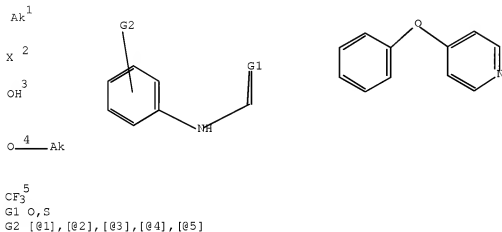


=&gt; d his 178

(FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008)

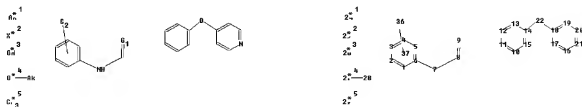
L78 5 S L77 NOT L54

=&gt; d que 178

L1 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20070142440/PN  
L47 STR

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

exact/norm bonds :

6-7 7-8 8-9 14-22 18-22 27-28

normalized bonds :  
 1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21  
 17-18 18-19 19-20 20-21  
 isolated ring systems :  
 containing 1 : 10 : 16 :

G1:0,S

G2:[\*1],[\*2],[\*3],[\*4],[\*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom  
 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom  
 20:Atom 21:Atom  
 22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS  
 37:Atom

L48 SCR 2043 AND 1918 AND 2050  
 L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48  
 L52 607 SEA FILE=HCAPLUS ABB=ON PLU=ON L50  
 L53 584 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX  
 L54 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004  
 OR PRY<2004)  
 L69 22 SEA FILE=HCAPLUS ABB=ON PLU=ON BURGDORF L2/AU  
 L70 45 SEA FILE=HCAPLUS ABB=ON PLU=ON BUCHSTALLER H2/AU  
 L71 36 SEA FILE=HCAPLUS ABB=ON PLU=ON STIEBER F2/AU  
 L72 28 SEA FILE=HCAPLUS ABB=ON PLU=ON AMENDT C2/AU  
 L73 202 SEA FILE=HCAPLUS ABB=ON PLU=ON GREINER H2/AU  
 L74 150 SEA FILE=HCAPLUS ABB=ON PLU=ON GRELL M2/AU  
 L75 38 SEA FILE=HCAPLUS ABB=ON PLU=ON SIRRENBERG C2/AU  
 L76 3 SEA FILE=HCAPLUS ABB=ON PLU=ON ZENKE K2/AU  
 L77 10 SEA FILE=HCAPLUS ABB=ON PLU=ON (((L69 OR L70 OR L71 OR L72  
 OR L73 OR L74 OR L75 OR L76)) AND L52) OR (L1 AND L52)  
 L78 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L77 NOT L54

=> d his l107

(FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:48:43 ON 16 JUL 2008)  
 L107 3 S (L100-L106) AND TYROSINE KINASE?

=> d que l107

L100 9 SEA BUCHSTALLER HANS PETER/AU  
 L101 8 SEA STIEBER FRANK/AU  
 L102 7 SEA AMENDT CHRISTIANE/AU  
 L103 14 SEA GREINER HARTMUT/AU  
 L104 70 SEA GRELL MATTHIAS/AU  
 L105 19 SEA SIRRENBERG CHRISTIAN/AU  
 L106 2 SEA ZENKE FRANK/AU  
 L107 3 SEA ((L100 OR L101 OR L102 OR L103 OR L104 OR L105 OR L106))  
 AND TYROSINE KINASE?

=> dup rem l78 l107

FILE 'HCAPLUS' ENTERED AT 13:53:35 ON 16 JUL 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE 'MEDLINE' ENTERED AT 13:53:35 ON 16 JUL 2008

FILE 'EMBASE' ENTERED AT 13:53:35 ON 16 JUL 2008

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PROCESSING COMPLETED FOR L78

PROCESSING COMPLETED FOR L107

L109 8 DUP REM L78 L107 (0 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE HCAPLUS

ANSWERS '6-7' FROM FILE MEDLINE

ANSWER '8' FROM FILE EMBASE

=> d l109 1-5 ibib abs; d l109 6-8 ibib ab

L109 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:817202 HCAPLUS Full-text

DOCUMENT NUMBER: 147:158473

TITLE: Use of integrin ligands and co-therapeutic agents for isolated organ perfusion combination therapy of cancer

INVENTOR(S): Goodman, Simon; Grell, Matthias; Ten Hagen,

Timo L. M.; Egermont, Alexander M. M.

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 54pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082742	A1	20070726	WO 2007-EP408	20070118
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.:

EP 2006-1049

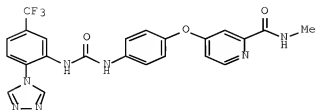
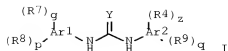
A 20060118

AB The invention discloses a combination therapy for the treatment of tumors and tumor metastases comprising administration of integrin ligands, preferably integrin antagonists, together with co-therapeutic agents or therapy forms that have synergistic efficacy when administered together with the ligands, such as chemotherapeutic agents and/or radiation therapy, in isolated organ perfusion. The therapy results in a synergistic potential increase of the inhibition effect of each individual therapeutic on tumor cell proliferation, yielding more effective treatment than found by administering an individual component alone.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L109 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2006:364321 HCAPLUS Full-text  
 DOCUMENT NUMBER: 144:412515  
 TITLE: Heterocyclic substituted bisarylurea derivatives as  
 kinase inhibitors and their preparation,  
 pharmaceutical compositions, and use for treatment of  
 diseases mediated or propagated by kinases  
 INVENTOR(S): Stieber, Frank; Jonczyk, Alfred; Hoelzemann,  
 Guenter; Buchstaller, Hans-Peter;  
 Burgdorf, Lars Thore; Rautenberg, Wilfried;  
 Greiner, Hartmut  
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany  
 SOURCE: PCT Int. Appl., 232 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006040056	A1	20060420	WO 2005-EP10744	20051006
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2005293839	A1	20060420	AU 2005-293839	20051006
CA 2584185	A1	20060420	CA 2005-2584185	20051006
EP 1799669	A1	20070627	EP 2005-789864	20051006
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
CN 101039932	A	20070919	CN 2005-80035117	20051006
JP 2008515943	T	20080515	JP 2007-536047	20051006
MX 200704248	A	20070612	MX 2007-4248	20070410
KR 2007062998	A	20070618	KR 2007-708364	20070412
IN 2007KN01680	A	20070727	IN 2007-KN1680	20070511
PRIORITY APPLN. INFO.:			EP 2004-24369	A 20041013
			EP 2005-16845	A 20050803
			WO 2005-EP10744	W 20051006
OTHER SOURCE(S):	MARPAT 144:412515			
GI				



II

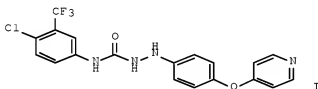
AB The invention relates to heterocyclic substituted bisarylurea derivs. of formula I, the use of the compds. of formula I as inhibitors of one or more kinases, the use of the compds. of formula I for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Compds. of formula I wherein R<sub>4</sub> is (X-Ar3) $\alpha$ -(R10)<sub>10</sub>; Ar<sub>1</sub>, Ar<sub>2</sub>, and Ar<sub>3</sub> are independently 5- to 14-membered unsatd. or aromatic cyclic hydrocarbon, or 2- to 10-membered unsatd. or aromatic heterocyclic residue, preferably 1 to 5 heteroatoms selected from N, O, and S;  $\alpha$  is 0, 1, or 2; r, z, and p are independently 0, 1, 2, 3, 4 or 5; R<sub>7</sub> is nitrogen containing heterocyclic moiety bound directly to Ar<sub>1</sub> via a nitrogen atom, etc.; R<sub>8</sub>, R<sub>9</sub>, and R<sub>10</sub> are independently H, (alkoxy)alkyl, alkenyl, C<sub>3</sub>-7 cycloalkyl, alkenylcycloalkyl, halo, CH<sub>2</sub>halo, CH(halo)<sub>2</sub>, C(halo)<sub>3</sub>, NO<sub>2</sub>, etc.; Y is O, S, NH and derivs., (un)substituted CHNO<sub>2</sub>, (un)substituted CHCN, or C(CN)<sub>2</sub>; g is 1, 2, or 3; q is 0, 1, 2, 3 or 4; and their pharmaceutically acceptable derivs., salts and solvates thereof are claimed in this invention. Example compound II was prepared by chlorination and esterification of pyridine-2-carboxylic acid to give Me 4-chloropyridine-2-carboxylate, which underwent amidation with methylamine to give 4-chloropyridine-2-carboxylic acid methylamide, which was reacted with 4-aminophenol; the resulting 4-(4-aminophenoxy)pyridine-2-carboxylic acid methylamine reacted with p-nitrophenyl chloroformate and 4-(2-amino-4-trifluoromethylphenyl)-1,2,4-triazole to give example compound II. All the invention compds. were evaluated for their activity as modulators and inhibitors of kinases. From the assay, it was determined that these compds. preferably inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in cultures with IC<sub>50</sub> values of 0.01-5.0  $\mu$ M.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

1109 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:977019 HCAPLUS Full-text  
 DOCUMENT NUMBER: 143:286162  
 TITLE: Preparation of aryl semicarbazide derivatives as  
 kinase inhibitors  
 INVENTOR(S): Buchstaller, Hans-Peter; Finsinger, Dirk;  
 Stieber, Frank; Wiesner, Matthias;  
 Amendt, Christiane; Sirrenberg,  
 Christian; Zenke, Frank; Grell, Matthias  
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany  
 SOURCE: PCT Int. Appl., 278 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082853	A1	20050909	WO 2005-EP1443	20050214
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2005217041	A1	20050909	AU 2005-217041	20050214
CA 2557359	A1	20050909	CA 2005-2557359	20050214
EP 1727800	A1	20061206	EP 2005-715319	20050214
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR			
JP 2007523928	T	20070823	JP 2007-500096	20050214
PRIORITY APPLN. INFO.:			EP 2004-4330	A 20040226
			WO 2005-EP1443	W 20050214
OTHER SOURCE(S):		CASREACT 143:286162; MARPAT 143:286162		
GI				

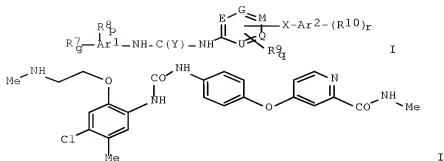


AB Title compds. of formula A-D-B [D = bivalent semicarbazide moiety, or a derivative thereof; A = (un)substituted moiety L-(M-L1)<sub>n</sub> where L = 5-7 membered cyclic structure, preferably selected from the group consisting of aryl, heteroaryl, arylene, and heteroarylene, bound directly to D, L1 = (un)substituted cyclic moiety preferably selected from aryl, heteroaryl, aralkyl, cycloalkyl, and heterocyclyl, M = bond or bridging group, n = 0-4; B = (un)substituted, up to tricyclic aryl or heteroaryl moiety], and their pharmaceutically acceptable salts are prepared and disclosed as inhibitors of one or more kinases (no data). Thus, e.g., I was prepared by reaction of 4-chloro-3-trifluoromethylphenyl isocyanate with 4-(pyridin-4-yloxy)phenylhydrazine (preparation given). Further disclosures include the use of the compds. of the invention for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L109 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:823661 HCAPLUS Full-text  
 DOCUMENT NUMBER: 143:229726  
 TITLE: Preparation of 1,3-diarylureas as inhibitors of raf  
 and other kinases useful against cancer and other  
 diseases  
 INVENTOR(S): Eochstaller, Hans-Peter; Burgdorf,  
 Lars; Stieber, Frank; Amendt,  
 Christiane; Grell, Matthias;  
 Sirrenberg, Christian; Zenke, Frank  
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany  
 SOURCE: PCT Int. Appl., 264 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075425	A2	20050818	WO 2005-EP387	20050117
WO 2005075425	A3	20061214		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2005211448	A1	20050818	AU 2005-211448	20050117
CA 2554878	A1	20050818	CA 2005-2554878	20050117
EP 1730111	A2	20061213	EP 2005-700967	20050117
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU			
CN 1972925	A	20070530	CN 2005-80002901	20050117
BR 2005007198	A	20070626	BR 2005-7198	20050117
JP 2007519653	T	20070719	JP 2006-549997	20050117
US 20070161677	A1	20070712	US 2006-587292	20060725
MX 2006PA08449	A	20061002	MX 2006-PA8449	20060726
IN 2006KN02441	A	20070525	IN 2006-KN2441	20060828
PRIORITY APPLN. INFO.:			EP 2004-2092	A 20040130
			WO 2005-EP387	W 20050117
OTHER SOURCE(S):	MARPAT 143:229726			
GI				



AB The present invention relates to bisaryleurea derivs. (shown as I; variables defined below; e.g. 4-[4-[3-[4-chloro-5-methyl-2-(2-methylaminoethoxy)phenyl]ureido]phenoxy]pyridine-2-carboxylic acid methylamide (shown as II)), their use as inhibitors of raf-kinase (no data) and for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Methods of preparation are claimed and >100 example preps. are included. For example, 1-[2-[2-[(tert-butoxycarbonyl)(methyl)amino]ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea was prepared (87 %) by reacting tert-Bu [2-[2-amino-4-(trifluoromethyl)phenoxy]ethyl](methyl)carbamate (preparation given) with p-nitrophenyl chloroformate followed by N-methyl-4-(4-aminophenoxy)pyridine-2-carboxamide (preparation given) and DIPEA; deprotection gave 86 % 1-[2-[2-(methylamino)ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea. For I: Ar1, Ar2 = aromatic hydrocarbons containing 6 to 14 C atoms and ethylenic unsatd. or aromatic heterocyclic residues containing 3 to 10 C atoms and one or two heteroatoms, = N, O and S; E, G, M, Q and U = C and N atoms, with the proviso that  $\geq 1$  of E, G, M, Q and U are C atoms and that X is bonded to a C atom. R7 = Het, OHet, N(R11)Het, (CR5R6)kHet, et al. or R7 = -SO2-CR8:CR8-, wherein both valencies are bound vicinally to Ar1; R8, R9 and R10 = H, A, cycloalkyl comprising 3 to 7 C atoms, Hal, et al.; Y = O, S, NR21, C(R22)-NO2, C(R22)-CN and C(CN)2; g = 1-3, preferably 1 or 2, p, r = 0-5; q = 0-4, preferably 0, 1 or 2; addnl. details are given in the claims.

L109 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:982303 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 143:286291

TITLE: Preparation of 2-pyridinecarboxamides as kinase inhibitors

INVENTOR(S): Burgorf, Lars; Buchstaller, Hans-Peter; Stieber, Frank; Amendt, Christiane; Grsiner, Hartmut; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Ger. Offen., 33 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

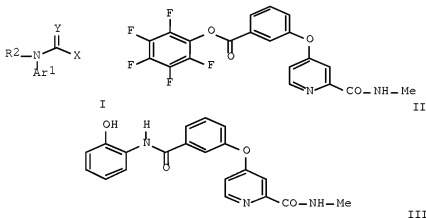
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:



PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102004009238	A1	20050908	DE 2004-102004009238	20040226
AU 2005219496	A1	20050915	AU 2005-219496	20050113
CA 2557302	A1	20050915	CA 2005-2557302	20050113
WO 2005085202	A1	20050915	WO 2005-EP273	20050113
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1718614	A1	20061108	EP 2005-700886	20050113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
JP 2007523921	T	20070823	JP 2007-500077	20050113
US 20070142440	A1	20070621	US 2006-590724	20060825 <--
PRIORITY APPLN. INFO.:				
			DE 2004-102004009238A	20040226
			WO 2005-EP273	W 20050113
OTHER SOURCE(S):				
GI				
MARPAT 143:286291				



AB Title compds. I [X = Ar2-Z-Ar3; Ar1, Ar2, Ar3 = (un)substituted aromatic, het; R1 = H, aryl, O-aryl, etc.; R2 = H, A, alkylene-aryl, etc.; A = alkyl with provisos; Z = Gln, GlnEG2m, EGlnG2m, etc.; E = O, CO, C=N, etc.; G1, G2 = CR1R1, E; n = 0-5; m = 0-2] and their pharmaceutically acceptable salts and formulations were prepared. For example, N-alkylation of 2-aminophenol with pentafluorophenol II afforded pyridinecarboxamide III in 13% yield. Compds. I are claimed to be effective inhibitors of the tyrosine kinases, in particular TIE-2 and VEGFR, and the Raf kinases.

L109 ANSWER 6 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2003332773 MEDLINE [Full-text](#)  
 DOCUMENT NUMBER: PubMed ID: 12866072  
 TITLE: Multistep solid-phase synthesis of an antibiotic and  
 receptor tyrosine kinase inhibitors  
 using the traceless phenylhydrazide linker.  
 AUTHOR: Stieber Frank; Grether Uwe; Mazitschek Ralph;  
 Soric Natascha; Giannis Athanassios; Waldmann Herbert  
 CORPORATE SOURCE: Max-Planck-Institut für Molekulare Physiologie, Abteilung  
 Chemische Biologie, Otto-Hahn-Strasse 11, 44227 Dortmund,  
 Germany.  
 SOURCE: Chemistry (Weinheim an der Bergstrasse, Germany), (2003 Jul  
 21) Vol. 9, No. 14, pp. 3282-91.  
 Journal code: 9513783. ISSN: 0947-6539.  
 PUB. COUNTRY: Germany: Germany, Federal Republic of  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200309  
 ENTRY DATE: Entered STN: 17 Jul 2003  
 Last Updated on STN: 11 Sep 2003  
 Entered Medline: 10 Sep 2003  
 AB The hydrazide group is an oxidatively cleavable traceless linker for solid-  
 phase chemistry. This linker technology was used to develop a multistep  
 solid-phase synthesis of an antibiotic that is active against Mycobacterium  
 tuberculosis. Furthermore, we describe an efficient method for the traceless  
 synthesis of 2-aminothiazoles that display dual inhibitory activity against  
 the receptor tyrosine kinases VEGFR-2 and Tie-2. The synthesis method  
 proceeds through 9 steps on the solid phase and should give access to a much  
 larger library of 2-aminothiazoles, from which a new class of anti-  
 angiogenesis drugs may be developed.

L109 ANSWER 7 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2003043368 MEDLINE [Full-text](#)  
 DOCUMENT NUMBER: PubMed ID: 12481350  
 TITLE: Traceless solid-phase synthesis of 2-aminothiazoles:  
 receptor tyrosine kinase inhibitors  
 with dual selectivity for Tie-2 and VEGFR-2.  
 AUTHOR: Stieber Frank; Mazitschek Ralph; Soric Natascha;  
 Giannis Athanassios; Waldmann Herbert  
 CORPORATE SOURCE: Max-Planck-Institut für molekulare Physiologie, Abteilung  
 Chemische Biologie, Otto-Hahn-Strasse 11, 44227 Dortmund,  
 Germany.  
 SOURCE: Angewandte Chemie (International ed. in English), (2002 Dec  
 16) Vol. 41, No. 24, pp. 4757-61.  
 Journal code: 0370543. ISSN: 1433-7851.  
 PUB. COUNTRY: Germany: Germany, Federal Republic of  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 30 Jan 2003  
 Last Updated on STN: 19 Mar 2003  
 Entered Medline: 18 Mar 2003

L109 ANSWER 8 OF 8 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1996270766 EMBASE Full-text  
 TITLE: Neurotrophins stimulate the release of dopamine from rat mesencephalic neurons via Trk and p75(Lntr) receptors.  
 AUTHOR: Blochl, Andrea (correspondence); Sirrenberg, Christian  
 CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Department of Neurochemistry, D-82152 Martinsried, Germany. Bloechl@alf.biochem.mpg.de  
 AUTHOR: Blochl, Andrea (correspondence)  
 CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Dept. of Neurochemistry, Am Klopferspitz 18a, D-82152 Martinsried, Germany. Bloechl@alf.biochem.mpg.de  
 AUTHOR: Sirrenberg, Christian  
 CORPORATE SOURCE: Ludwig-Maximilian-University Munich, Dept. of Biochemistry, 80336 Munich, Germany.  
 AUTHOR: Blochl, Andrea (correspondence)  
 CORPORATE SOURCE: Dept. of Neurochemistry, Max-Planck-Institute for Psychiatry, Am Klopferspitz 18a, D-82152 Martinsried, Germany.  
 SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 35, pp. 21100-21107.  
 Refs: 64  
 ISSN: 0021-9258 CODEN: JBCHA3  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 029 Clinical and Experimental Biochemistry  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 7 Oct 1996  
 Last Updated on STN: 7 Oct 1996

AB We analyzed the short term effect of neurotrophins on mesencephalic neuronal cultures of embryonic (E14) rats with respect to which receptors mediate the actions. Brain-derived neurotrophic factor (BDNF) or neurotrophin-3 enhanced within minutes in a dose-dependent manner (2, 20, 100 ng/ml for 5 min) depolarization-induced (KCl, 30 mM 5 min) and basal dopamine release, but nerve growth factor (NGF) was only effective at high doses (100 ng/ml). The effect of BDNF, but not of NGF, was blocked by K252a or K252b. BDNF, but not NGF, phosphorylated trkB receptors. The NGF-induced, but not the BDNF-induced effect upon the release of dopamine was blocked by anti-p75 antibody MC192. C(2)-ceramide, an analogue of ceramide, the second messenger of the sphingomyelin pathway, and sphingomyelinase itself induced a release of dopamine comparable with the effect of NGF. NGF, but not BDNF, increased ceramide production. In addition, simultaneous treatment with BDNF and NGF led to a partial prevention of the NGF stimulated, p75(Lntr)-mediated effect. We conclude that BDNF stimulates the release of dopamine by activation of the trkB receptor, whereas NGF affects the release via the p75(Lntr) receptor inducing the sphingomyelin pathway.

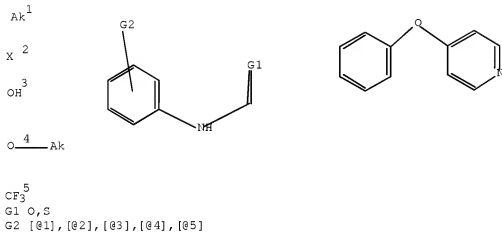
=> d his l54

(FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008)

L54 64 S L53 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d que l54

L47 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

exact/norm bonds :

6-7 7-8 8-9 14-22 18-22 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21

17-18 18-19 19-20 20-21

isolated ring systems :

containing 1 : 10 : 16 :

G1:O,S

G2:[\*1],[\*2],[\*3],[\*4],[\*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

20:Atom 21:Atom

22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS

37:Atom

L48 SCR 2043 AND 1918 AND 2050

L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48

L52 607 SEA FILE=HCAPLUS ABB=ON PLU=ON L50

L53 584 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX

L54 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L53 AND (AY&lt;2004 OR PY&lt;2004 OR PRY&lt;2004)

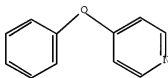
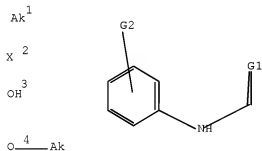
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L86 8 S L83 OR L85

=&gt; d que l86

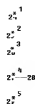
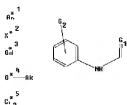
L47 STR



<sup>5</sup>CF<sub>3</sub>  
 G1 O,S  
 G2 [e1],[e2],[e3],[e4],[e5]

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



```

chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 7-8 8-9 14-22 18-22 27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 : 10 : 16 :

```

G1:O,S

G2:[\*1],[\*2],[\*3],[\*4],[\*5]

Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

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L48          SCR 2043 AND 1918 AND 2050
L50          1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
L64          1797 SEA FILE=HCAPLUS ABB=ON PLU=ON (TIE2 OR TIE(W)2 OR VEGFR OR
              RAP) (W) (KINASE? OR KINASE INHIB?)
L79          1 SEA FILE=REGISTRY ABB=ON PLU=ON L50 AND (MEDLINE/LC OR
              BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)
L81          89 SEA FILE=BIOSIS ABB=ON PLU=ON L79
L82          34 SEA FILE=BIOSIS ABB=ON PLU=ON L81 AND L64

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10/590724

L83 3 SEA FILE=BIOSIS ABB=ON PLU=ON L82 AND (PREP? OR SYNTHES?)  
 L85 6 SEA FILE=BIOSIS ABB=ON PLU=ON L82 AND TYROSINE KINASE?  
 L86 8 SEA FILE=BIOSIS ABB=ON PLU=ON L83 OR L85

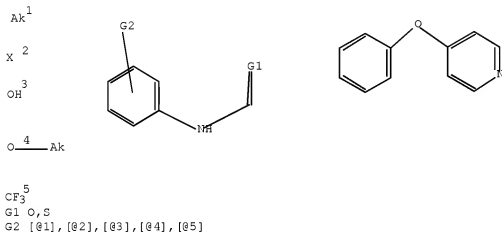
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L98 12 S L89 AND (AY<2004 OR PY<2004 OR PRY<2004)

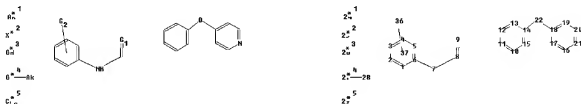
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L47 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str



chain nodes :

7 8 9 22 24 25 26 27 28 29 36

ring nodes :

1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21

chain bonds :

6-7 7-8 8-9 14-22 18-22 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-

21  
 17-18 18-19 19-20 20-21  
 exact/norm bonds :  
 6-7 7-8 8-9 14-22 18-22 27-28  
 normalized bonds :  
 1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21  
 17-18 18-19 19-20 20-21  
 isolated ring systems :  
 containing 1 : 10 : 16 :

G1:O,S

G2:[\*1],[\*2],[\*3],[\*4],[\*5]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom  
 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom  
 20:Atom 21:Atom  
 22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS  
 37:Atom

L48 SCR 2043 AND 1918 AND 2050  
 L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48  
 L79 1 SEA FILE=REGISTRY ABB=ON PLU=ON L50 AND (MEDLINE/LC OR  
 BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)  
 L88 2050 SEA FILE=EMBASE ABB=ON PLU=ON L79  
 L89 605 SEA FILE=EMBASE ABB=ON PLU=ON L88 AND TYROSINE KINASE?  
 L98 12 SEA FILE=EMBASE ABB=ON PLU=ON L89 AND (AY<2004 OR PY<2004 OR  
 PRY<2004)

=> dup rem 154 186 198

FILE 'HCAPLUS' ENTERED AT 13:54:57 ON 16 JUL 2008  
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 PROCESSING COMPLETED FOR L54  
 PROCESSING COMPLETED FOR L86  
 PROCESSING COMPLETED FOR L98

L110 84 DUP REM L54 L86 L98 (0 DUPLICATES REMOVED)  
 ANSWERS '1-64' FROM FILE HCAPLUS  
 ANSWERS '65-72' FROM FILE BIOSIS  
 ANSWERS '73-84' FROM FILE EMBASE

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L110 ANSWER 1 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2007:863627 HCAPLUS Full-text  
 DOCUMENT NUMBER: 147:235192



TITLE: Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis

INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Ken-Ichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshida, Takako; Suzuki, Yasuyuki; Arimoto, Itaru

PATENT ASSIGNEE(S): Eisai Co., Ltd, Japan

SOURCE: U.S., 458pp., Cont.-in-part of Appl. No. PCT/JP01/09221.

CODEN: USXXAM

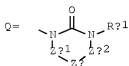
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7253286	B2	20070807	US 2003-420466	20030418 <--
US 20040053908	A1	20040318		
WO 2002032872	A1	20020425	WO 2001-JP9221	20011019 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1506962	B1	20080702		
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CN 101029022	A	20070905	CN 2007-10007097	20011019 <--
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US 20060160832	A1	20060720	US 2006-347749	20060203 <--
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JP 2000-320420				
JP 2000-386195				
JP 2001-46685				
WO 2001-JP9221				
AU 2001-295986				
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US 2003-420466  
US 2005-293785A3 20030418 <--  
A1 20051202OTHER SOURCE(S): MARPAT 147:235192  
GI

AB N-aryl or N-heteroaryleurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2)faCH:CH(CH2)fb (fa, fb = 0, 1, 2, 3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared. These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4-benzoyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzoyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropyleurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropyleurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT 417714-74-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

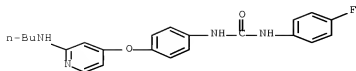
(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-74-0 HCAPLUS

CN Urea, N-[4-[2-(butylamino)-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)-  
(CA INDEX NAME)



INCL 546153000; 546155000; 514312000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 27, 63

IT	398487-65-5P	417712-82-4P	417712-83-5P	417712-84-6P	417712-85-7P
	417712-86-8P	417712-87-9P	417712-88-0P	417712-89-1P	417712-90-4P
	417712-91-5P	417712-92-6P	417712-93-7P	417712-94-8P	417712-95-9P
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	417713-01-0P	417713-02-1P	417713-03-2P	417713-04-3P	417713-05-4P
	417713-06-5P	417713-08-7P	417713-11-2P	417713-12-3P	417713-13-4P
	417713-14-5P	417713-15-6P	417713-16-7P	417713-17-8P	417713-18-9P
	417713-19-0P	417713-20-3P	417713-21-4P	417713-23-6P	417713-25-8P
	417713-26-9P	417713-27-0P	417713-28-1P	417713-29-2P	417713-30-5P
	417713-31-6P	417713-32-7P	417713-33-8P	417713-34-9P	417713-35-0P
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	417714-15-9P	417714-16-0P	417714-17-1P	417714-18-2P	417714-19-3P
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	417714-30-8P	417714-31-9P	417714-32-0P	417714-33-1P	417714-36-4P
	417714-37-5P	417714-38-6P	417714-39-7P	417714-40-0P	417714-41-1P
	417714-42-2P	417714-43-3P	417714-44-4P	417714-45-5P	417714-46-6P
	417714-47-7P	417714-48-8P	417714-49-9P	417714-50-2P	417714-51-3P
	417714-52-4P	417714-53-5P	417714-54-6P	417714-55-7P	417714-58-0P
	417714-59-1P	417714-60-4P	417714-62-6P	417714-63-7P	417714-64-8P
	417714-65-9P	417714-66-0P	417714-67-1P	417714-68-2P	417714-69-3P
	417714-70-6P	417714-71-7P	417714-72-8P	417714-73-9P	
	417714-74-0P	417714-75-1P	417714-76-2P	417714-77-3P	
	417714-78-4P	417714-79-5P	417714-80-8P	417714-81-9P	
	417714-82-0P	417714-83-1P	417714-84-2P	417714-85-3P	417714-86-4P
	417714-87-5P	417714-89-7P	417714-90-0P	417714-91-1P	417714-92-2P
	417714-93-3P	417714-94-4P	417714-95-5P	417714-96-6P	
	417714-97-7P	417714-98-8P	417714-99-9P	417715-00-5P	
	417715-01-6P	417715-02-7P	417715-03-8P	417715-05-0P	417715-07-2P
	417715-08-3P	417715-09-4P	417715-10-7P	417715-11-8P	417715-12-9P
	417715-13-0P	417715-14-1P	417715-15-2P	417715-16-3P	417715-17-4P
	417715-18-5P	417715-19-6P	417715-20-9P	417715-21-0P	417715-22-1P
	417715-23-2P	417715-24-3P	417715-25-4P	417715-27-6P	417715-28-7P
	417715-29-8P	417715-30-1P	417715-31-2P	417715-32-3P	417715-33-4P
	417715-34-5P	417715-35-6P	417715-36-7P	417715-37-8P	417715-39-0P
	417715-40-3P	417715-42-5P	417715-44-7P	417715-46-9P	417715-47-0P
	417715-49-2P	417715-51-6P	417715-53-8P	417715-55-0P	417715-57-2P
	417715-59-4P	417715-61-8P	417715-63-0P	417715-65-2P	417715-66-3P
	417715-67-4P	417715-68-5P	417715-69-6P	417715-70-9P	

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

IT	417715-71-0P	417715-72-1P	417715-73-2P	417715-74-3P	417715-75-4P
	417715-76-5P	417715-77-6P	417715-78-7P	417715-79-8P	417715-81-2P
	417715-83-4P	417715-85-6P	417715-86-7P	417715-88-9P	417715-90-3P
	417715-91-4P	417715-93-6P	417715-95-8P	417715-97-0P	417715-99-2P
	417716-01-9P	417716-03-1P	417716-05-3P	417716-06-4P	417716-07-5P
	417716-08-6P	417716-09-7P	417716-10-0P	417716-12-2P	417716-13-3P
	417716-14-4P	417716-15-5P	417716-16-6P	417716-17-7P	417716-18-8P
	417716-19-9P	417716-20-2P	417716-21-3P	417716-22-4P	417716-23-5P
	417716-24-6P	417716-25-7P	417716-26-8P	417716-27-9P	417716-28-0P
	417716-29-1P	417716-30-4P	417716-31-5P	417716-32-6P	417716-33-7P
	417716-34-8P	417716-35-9P	417716-36-0P	417716-37-1P	417716-38-2P
	417716-39-3P	417716-40-6P	417716-41-7P	417716-43-9P	417716-44-0P
	417716-45-1P	417716-46-2P	417716-47-3P	417716-48-4P	417716-49-5P
	417716-50-8P	417716-51-9P	417716-52-0P	417716-53-1P	417716-54-2P
	417716-55-3P	417716-56-4P	417716-57-5P	417716-58-6P	417716-59-7P
	417716-60-0P	417716-61-1P	417716-62-2P	417716-63-3P	417716-64-4P
	417716-65-5P	417716-66-6P	417716-67-7P	417716-68-8P	417716-69-9P
	417716-70-2P	417716-71-3P	417716-72-4P	417716-73-5P	417716-74-6P
	417716-75-7P	417716-76-8P	417716-77-9P	417716-78-0P	417716-79-1P
	417716-80-4P	417716-81-5P	417716-82-6P	417716-83-7P	417716-84-8P
	417716-85-9P	417716-86-0P	417716-87-1P	417716-88-2P	417716-89-3P
	417716-90-6P	417716-91-7P	417716-92-8P	417716-93-9P	417716-94-0P
	417716-95-1P	417716-96-2P	417716-97-3P	417716-98-4P	417716-99-5P
	417717-00-1P	417717-01-2P	417717-02-3P	417717-03-4P	417717-04-5P
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	417717-10-3P	417717-11-4P	417717-14-7P	417717-15-8P	417717-16-9P
	417717-17-0P	417717-18-1P	417717-19-2P	417717-20-5P	417717-22-7P
	417717-23-8P	417717-24-9P	417717-25-0P	417717-26-1P	417717-27-2P
	417717-28-3P	417717-29-4P	417717-30-7P	417717-31-8P	417717-32-9P
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	417717-38-5P	417717-40-9P	417717-41-0P	417717-43-2P	417717-44-3P
	417717-46-5P	417717-47-6P	417717-48-7P	417717-49-8P	417717-51-2P
	417717-52-3P	417717-53-4P	417717-55-6P	417717-57-8P	417717-58-9P
	417717-60-3P	417717-62-5P	417717-63-6P	417717-64-7P	417717-66-9P
	417717-67-0P	417717-68-1P	417717-69-2P	417717-70-5P	417717-71-6P
	417717-72-7P	417717-73-8P	417717-74-9P	417717-75-0P	417717-76-1P
	417717-77-2P	417717-78-3P	417717-79-4P	417717-81-8P	417717-83-0P
	417717-86-3P	417717-87-4P	417717-88-5P	417717-89-6P	417717-93-2P
	417717-95-4P	417717-97-6P	417717-99-8P	417718-00-4P	417718-02-6P
	417718-04-8P	417718-06-0P	417718-10-6P	417718-11-7P	
	417718-13-9P	417718-15-1P	417718-17-3P		
	417718-19-5P	417718-21-9P	417718-23-1P	417718-25-3P	
	417718-26-4P	417718-28-6P	417718-30-0P	417718-31-1P	417718-32-2P
	417718-34-4P	417718-35-5P	417718-36-6P	417718-37-7P	417718-39-9P
	417718-40-2P	417718-41-3P	417718-42-4P	417718-43-5P	417718-44-6P
	417718-45-7P	417718-46-8P	417718-47-9P	417718-48-0P	417718-49-1P
	417718-50-4P	417718-51-5P	417718-52-6P	417718-53-7P	417718-54-8P
	417718-55-9P	417718-56-0P	417718-57-1P		

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

IT	399-95-1P	3898-47-3P	4792-60-3P	5264-02-8P	6980-08-1P	7251-09-4P
	14549-38-3P	17424-90-7P	17576-39-5P	17614-10-7P	18031-97-5P	
	39142-40-0P	65141-00-6P	65141-04-0P	74889-21-7P	81479-55-2P	
	96783-89-0P	97480-55-2P	105130-28-7P	124041-03-8P	130035-46-0P	
	185220-68-2P	190060-72-1P	221040-07-9P	286371-87-7P	347151-53-5P	
	417720-95-7P	417720-96-8P	417720-97-9P	417720-98-0P	417720-99-1P	
	417721-00-7P	417721-01-8P	417721-02-9P	417721-03-0P	417721-04-1P	
	417721-05-2P	417721-06-3P	417721-07-4P	417721-08-5P	417721-09-6P	
	417721-10-9P	417721-11-0P	417721-12-1P	417721-13-2P	417721-14-3P	
	417721-15-4P	417721-16-5P	417721-17-6P	417721-18-7P	417721-19-8P	
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	417721-25-6P	417721-26-7P	417721-27-8P	417721-28-9P	417721-29-0P	
	417721-30-3P	417721-31-4P	417721-32-5P	417721-33-6P	417721-34-7P	
	417721-35-8P	417721-36-9P	417721-37-0P	417721-38-1P	417721-39-2P	
	417721-40-5P	417721-41-6P	417721-42-7P	417721-43-8P	417721-44-9P	
	417721-45-0P	417721-46-1P	417721-47-2P	417721-48-3P	417721-49-4P	
	417721-50-7P	417721-51-8P	417721-52-9P	417721-53-0P	417721-54-1P	
	417721-55-2P	417721-56-3P	417721-57-4P	417721-58-5P	417721-59-6P	
	417721-60-9P	417721-61-0P	417721-62-1P	417721-63-2P	417721-64-3P	
	417721-65-4P	417721-66-5P	417721-67-6P	417721-68-7P	417721-69-8P	
	417721-70-1P	417721-71-2P	417721-72-3P	417721-73-4P	417721-74-5P	
	417721-75-6P	417721-76-7P	417721-77-8P	417721-78-9P		
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	417721-83-6P	417721-84-7P	417721-85-8P	417721-86-9P	417721-87-0P	
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	417721-93-8P	417721-94-9P	417721-95-0P	417721-96-1P		
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	417722-02-2P	417722-03-3P	417722-04-4P	417722-05-5P		
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	417722-42-0P	417722-43-1P	417722-44-2P	417722-45-3P	417722-46-4P	
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	417722-57-7P	417722-58-8P	417722-59-9P	417722-60-2P	417722-61-3P	
	417722-62-4P	417722-63-5P	417722-64-6P	417722-65-7P	417722-66-8P	
	417722-67-9P	417722-69-1P	417722-71-5P	417722-73-7P	417722-75-9P	
	417722-76-0P	417722-77-1P	417722-78-2P	417722-79-3P	417722-81-7P	
	417722-82-8P	417722-83-9P	417722-85-1P	417722-87-3P	417722-89-5P	
	417722-91-9P	417722-93-1P	417722-95-3P	417722-97-5P	417722-99-7P	
	417723-01-4P	417723-03-6P	417723-05-8P	417723-07-0P	417723-09-2P	
	417723-11-6P	417723-13-8P	417723-15-0P	417723-17-2P	417723-19-4P	
	417723-21-8P	417723-23-0P	417723-25-2P	417723-27-4P	417723-29-6P	
	417723-31-0P	417723-33-2P	417723-35-4P	417723-37-6P		

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation of urea derivs. containing nitrogenous aromatic ring compds.)

as

angiogenesis inhibitors for prevention or treatment of diseases)

IT	417723-39-8P	417723-41-2P	417723-43-4P	417723-44-5P	417723-45-6P
	417723-49-0P	417723-51-4P	417723-53-6P	417723-54-7P	
	417723-55-8P	417723-56-9P	417723-57-0P	417723-58-1P	417723-59-2P
	417723-60-5P	417723-61-6P	417723-62-7P	417723-63-8P	417723-64-9P
	417723-65-0P	417723-66-1P	417723-67-2P	417723-68-3P	417723-70-7P
	417723-71-8P	417723-72-9P	417723-73-0P	417723-74-1P	417723-75-2P
	417723-76-3P	417723-77-4P	417723-78-5P	417723-80-9P	417723-81-0P

417723-82-1P	417723-83-2P	417723-84-3P	417723-85-4P	417723-87-6P
417723-89-8P	417723-91-2P	417723-93-4P	417723-94-5P	417723-95-6P
417723-96-7P	417723-97-8P	417723-98-9P	417723-99-0P	417724-00-6P
417724-01-7P	417724-02-8P	417724-03-9P	417724-04-0P	417724-05-1P
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417724-11-9P	417724-12-0P	417724-13-1P	417724-14-2P	417724-15-3P
417724-16-4P	417724-17-5P	417724-18-6P	417724-19-7P	417724-20-0P
417724-21-1P	417724-24-4P	417724-25-5P	417724-26-6P	417724-27-7P
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417724-43-7P	417724-44-8P	417724-45-9P	417724-46-0P	417724-47-1P
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417724-92-6P	417724-94-8P	417724-95-9P	417724-96-0P	417724-98-2P
417724-99-3P	417725-00-9P	417725-01-0P	417725-02-1P	417725-05-4P
417725-08-7P	417725-09-8P			

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 2 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:691680 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 147:118041

TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: U.S., 52pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7235576	B1	20070626	US 2002-42203	20020111 <--
US 20030144278	A1	20030731	US 2002-283248	20021030 <--
US 20080108672	A1	20080508	US 2007-768104	20070625 <--
PRIORITY APPLN. INFO.:			US 2001-367380P	P 20010112 <--
			US 2002-42203	A1 20020111 <--

OTHER SOURCE(S): MARPAT 147:118041

AB Aryl ureas A-NHCONH-B [A, B = C5-40 (poly)aryl, optionally containing 0-4 N, O, S heteroatoms, optionally substituted by (hetero)aryl, (hetero)aryloxy, halo, cyano, nitro, alkoxy, alkylthio, amino, hydroxyalkyl, sulfo, acyl, carboxamido-groups], useful as Raf-kinase inhibitors for treatment and

inhibition of cancerous cell growth, were prepared by standard synthetic procedures by reactions of the corresponding isocyanates with aromatic amines and tested for inhibition of Raf kinase and growth of human tumor cell lines HCT116 and DLD-1, exhibiting IC50 values of 1 nM to 10  $\mu$ M. In an example, N-(4-chloro-3-trifluoromethylphenyl)-N'-[4-(2-methylaminocarbonyl-4-pyridinyloxy)phenyl]urea was prepared by reaction of 65.9 mmol of 4-chloro-3-trifluoromethylphenyl isocyanate with 65.77 mmol of 4-(2-methylaminocarbonyl-4-pyridinyloxy)aniline in CH2Cl2 at room temperature for 22 h with 93% yield.

IT 943024-26-8P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

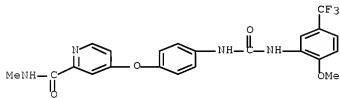
RN 943024-26-8 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 284461-44-5

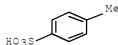
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CM 2

CRN 104-15-4

CMF C7 H8 O3 S



INCL 514388000; 514354000; 514358000; 514597000; 514552000; 546329000; 546339000; 564054000; 564055000; 564336000

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 63

IT 943024-26-8P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

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943024-29-1P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

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RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

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RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

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RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors

for treatment and inhibition of cancerous cell growth)

REFERENCE COUNT: 223 THERE ARE 223 CITED REFERENCES AVAILABLE FOR  
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L110 ANSWER 3 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1314363 HCAPLUS Full-text

DOCUMENT NUMBER: 144:57544

TITLE: Antibody drug conjugates and uses for cancer therapy

INVENTOR(S): Ebens, Allen J., Jr.; Jacobson, Frederic S.; Polakis,  
 Paul; Schwall, Ralph H.; Sliwowski, Mark X.; Spencer,  
 Susan D.

PATENT ASSIGNEE(S): Genentech, Inc., USA

SOURCE: PCI Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 160

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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			AU 2000-17482	A3 19991130 <--
			AU 2000-17499	A3 19991202 <--

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AU 2001-271938	A3 20010710 <--
AU 2001-71938	T0 20010710 <--
US 2001-927796	B1 20010809 <--
WO 2001-US26626	W 20010823 <--
US 2001-990711	A1 20011114 <--
US 2001-992521	B1 20011114 <--
WO 2001-US48938	W 20011213 <--
US 2002-52586	A1 20020115 <--
WO 2002-US10513	W 20020403 <--
US 2002-123155	A1 20020415 <--
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US 2002-145627	A1 20020514 <--
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US 2002-197942	B1 20020718 <--
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US 2002-199464	B1 20020719 <--
US 2002-211858	A1 20020802 <--
AU 2002-330015	A3 20020911 <--
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AU 2003-200137	A3 20030115 <--
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AU 2003-261484	A 20031106 <--
US 2003-520842P	P 20031117 <--
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AU 2005-200179	A3 20050114
US 2005-141344	A2 20050531
WO 2005-US18829	W 20050531
US 2006-461752	A2 20060801

OTHER SOURCE(S): MARPAT 144:5/544

AB The present invention relates to antibody-drug conjugate compds. with a formula of Ab-(L-D)p where 1 to 8 (p) maytansinoid drug moieties (D) are covalently linked by L to an antibody (Ab) which binds to an ErbB receptor, or which binds to one or more tumor-associated antigens or cell-surface receptors. These compds. may be used in methods of diagnosis or treatment of cancer, and other diseases and disorders.

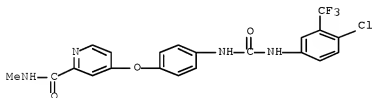
IT 284461-73-0, Sorafenib

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibody drug conjugates and uses for cancer therapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K047-48

ICS A61P035-00; G01N033-574

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 15

IT 51-21-8, 5-FU 58-05-9, Leucovorin 4856-87-5 5132-30-9 28537-70-4, 1,4-Bis-maleimidobutane 53123-88-9, Rapamycin 61825-94-3, Oxaliplatin 64987-85-5, SMCC 71865-37-7 86099-06-1 112809-51-5, Letrozole 115597-84-7 129453-61-8, Fulvestrant 179324-69-7, Bortezomib 180288-69-1, Trastuzumab 183321-74-6, Erlotinib 184475-35-2, Gefitinib 189013-00-1 193275-84-2, Lonafarnib 212142-18-2, ZK222584 216974-75-3, Bevacizumab 220127-57-1, Imatinib mesylate 231277-92-2, Lapatinib 284461-73-0, Sorafenib 557795-19-4, Sutent

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibody drug conjugates and uses for cancer therapy)

L110 ANSWER 4 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:470256 HCAPLUS Full-text

DOCUMENT NUMBER: 143:20052

TITLE: Urea derivatives as kinase modulators

INVENTOR(S): Milanov, Zdravko V.; Patel, Hitesh K.; Grotzfeld, Robert M.; Mehta, Shamal A.; Andiliy, Lai G.; Lockhart, David J.

PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA

SOURCE: PCT Int. Appl., 350 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005048948	A2	20050602	WO 2004-US38288	20041115 <--
WO 2005048948	A3	20050728		
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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US 20050148605	A1	20050707	US 2004-989745	20041115 <--
US 20050165031	A1	20050728	US 2004-989814	20041115 <--
US 20050165024	A1	20050728	US 2004-989824	20041115 <--
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US 20050171171	A1	20050804	US 2004-989766	20041115 <--
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US 20050267182	A1	20051201	US 2004-989717	20041115 <--
EP 1684762	A2	20060802	EP 2004-811122	20041115 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS			
JP 2007512255	T	20070517	JP 2006-539991	20041115 <--
PRIORITY APPLN. INFO.:			US 2003-520273P	P 20031113 <--
			US 2003-527094P	P 20031203 <--
			US 2003-531082P	P 20031218 <--
			US 2003-531243P	P 20031218 <--
			WO 2004-US38288	W 20041115

OTHER SOURCE(S): MARPAT 143:20052

AB The invention provides methods and compns. for treating conditions mediated by various kinases wherein derivs. of urea compds. are employed. The invention also provides methods of using the compds. and/or compns. in the treatment of a variety of diseases and unwanted conditions in subjects such as cellular proliferative disorders.

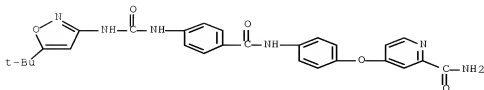
IT 852669-21-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (urea derivs. as kinase modulators for treatment of cellular proliferative disorders)

RN 852669-21-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-[[[5-(1,1-dimethylethyl)-3-isoazolyl]amino]carbonyl]amino]benzoyl]amino]phenoxy]- (CA INDEX NAME)





IC ICM A61K

CC 1-12 (Pharmacology)

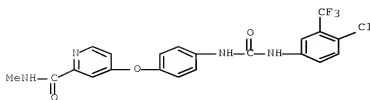
Section cross-reference(s): 7, 28

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 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (urea derivs. as kinase modulators for treatment of cellular  
 proliferative disorders)

L110 ANSWER 5 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:470251 HCAPLUS Full-text  
 DOCUMENT NUMBER: 143:19957  
 TITLE: Combination therapy comprising a cyclooxygenase 2  
 (COX-2) inhibitor and an antineoplastic agent for  
 treatment or prevention of neoplasia  
 INVENTOR(S): Masferrer, Jaime L.  
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA  
 SOURCE: PCT Int. Appl., 317 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

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WO 2005048942	A2	20050602	WO 2004-US38019	20041115 <--
WO 2005048942	A3	20060330		
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20050227929	A1	20051013	US 2004-989192	20041115 <--
PRIORITY APPLN. INFO.:			US 2003-519701P	P 20031113 <--
AB	A method for treating or preventing neoplasia or a neoplasia-related disorder in a subject is provided, the method comprising administering to the subject an effective amount of a combination comprising a COX-2 inhibitor and an antineoplastic agent.			
IT	284461-73-0, BAY 439006 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)			
RN	284461-73-0 HCAPLUS			
CN	2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)			



IC ICM A61K  
 CC 1-6 (Pharmacology)  
 IT 74-79-3D, L-Arginine, monomethyl derivs. 103-82-2D, Phenylacetic acid, derivs. 254-04-6D, Benzopyran, derivs. 355-25-9, NC 100100 646-08-2,  $\beta$ -Alethine 1400-61-9, Nystatin 1821-33-6 2353-33-5, 5-Aza-2'-deoxycytidine 5072-26-4, Buthionine sulfoximine 7689-03-4D, Camptothecin, glycoconjugate 9005-49-6, Dalteparin, biological studies 9014-42-0, RH-TPO 9074-87-7, Carboxypeptidase G2 18472-51-0, Oramed 19388-87-5, Taurolidine 33069-62-4, Paclitaxel 41941-56-4, Tocladesine 82855-09-2, Combretastatin 82952-64-5, Trimetrexate glucuronate 89778-26-7, GTX 006 97919-22-7 108560-70-9, Gallium maltolate 115427-51-5, INX-3280 118694-43-2, ILX 23-7553 128517-07-7 134774-45-1, Rasburicase 149882-10-0, Lurtotecan 152044-54-7, Epothilone B 152044-54-7D, Epothilone B, analogs 152459-95-5, Imatinib 156053-89-3, ADL 8-2698 160237-25-2, BMS-184476 162011-90-7, Rofecoxib 162635-04-3, CCI-779 169590-42-5, Celecoxib 170729-80-3, Aprepitant 172481-83-3, BMS 188797 173424-77-6, VNP-40101M 173937-91-2, Atrasentan 181695-72-7, Valdecoxib 186348-23-2, BAY 59-8862 188968-51-6, Cilengitide 191732-72-6, CDC 501 192391-48-3, Bexxar 192658-64-3 192819-27-5, CDC-801 195533-53-0, T-138067 195987-41-8 198470-84-7, Parecoxib 198470-85-8, Parecoxib sodium 198480-55-6, ERA 923 202409-33-4, Etoricoxib 205923-56-4, Cetuximab 209783-80-2, MS-275 209810-58-2, Aranesp 216503-58-1, BEC2 216974-75-3, Bevacizumab 219527-63-6, Repifermin 219989-84-1, BMS-247550 220578-59-6, Mylotarg 220991-20-8, Lumiracoxib 227619-96-7, CP-461 231277-92-2, GW-572016 236391-66-5, GTI 2040 236391-67-6, GTI 2501 246861-96-1, SB 251353 257933-82-7, EKB-569 259188-38-0, BMS-275291 261944-52-9 263351-82-2 267243-28-7 284461-72-0, BAY 439006 288392-69-8, MEDI-507 289499-45-2, CI-1033 321309-50-6, NC-100150 340014-19-9, Melacine 380907-94-8, Cytotoxin SS1(dsFv)-PE38 (synthetic) 428438-54-4, SPD 424 439153-64-7, CP 609754 447471-67-2, MG-98 543726-73-4, IMC 1C11 623174-20-9, ILX 651 791096-83-8, SD 01 845680-07-1, Lapuleucel-T 848866-33-1, T 900607 852286-49-8 852834-17-4, PK 412 852834-62-9D, TNT 1B, I131 labeled 852834-90-3, KSB 309 852834-96-9, SB 310 852835-00-8, NBI 3001 852835-01-9, APC 8020 852835-30-4, RK 0202 852835-36-0, SR 29142 852835-43-9, Stemgen 852835-52-0, ALVAC B 7.1 852835-53-1, GnRH Pharmaccine 852836-15-8, rV-MUC 1 852836-20-5, CapVax  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

L110 ANSWER 6 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

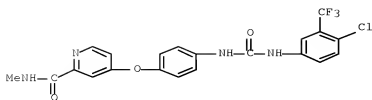
ACCESSION NUMBER: 2005:409543 HCAPLUS Full-text

DOCUMENT NUMBER: 142:457053

TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and

siRNA, and their use for enhancing apoptosis in cancer therapy  
 INVENTOR(S): Lacasse, Eric; McManus, Daniel  
 PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.  
 SOURCE: PCT Int. Appl., 112 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20050148535	A1	20050707	US 2004-975974	20041028 <--
CA 2542904	A1	20050512	CA 2004-2542904	20041029 <--
EP 1682565	A1	20060726	EP 2004-789809	20041029 <--
R:	DE, FR, GB			
JP 2007510408	T	20070426	JP 2006-537024	20041029 <--
PRIORITY APPLN. INFO.:			US 2003-516192P	P 20031030 <--
			WO 2004-CA1902	W 20041029
AB	The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).			
IT	284461-73-0, BAY-43-9006 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)			
RN	284461-73-0 HCAPLUS			
CN	2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)			



IC ICM C07H021-00  
 ICS A61K048-00; A61K031-7088; A61K031-713; A61P035-00; C12N015-85  
 CC 1-6 (Pharmacology)  
 Section cross-reference(s): 3, 6, 13, 14  
 IT 195612-80-7, Galarubicin 196488-72-9, Ranpirnase 199796-52-6,  
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 SU6668 257933-82-7, EKB-569 257938-36-6, ZD4190 259188-38-0,  
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 848874-02-2, Urocidin 849146-37-8, CTP-37 849146-41-4, Pentrix  
 849146-42-5, ISF-154 849148-55-6, Norelin 849148-82-9, TransMID-107  
 849148-97-6, MGW 849149-00-4, GMK 851343-54-9, 5-  
 Hydroxymethylidiscodermolide  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (human protein IAP (inhibitor of apoptosis protein) nucleobase  
 oligomers, including dsRNA, shRNA, and siRNA, and their use for  
 enhancing apoptosis in cancer therapy)

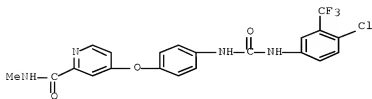
L110 ANSWER 7 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:409357 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 142:457052  
 TITLE: Sequences of antisense IAP (inhibitor of apoptosis

protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent  
 INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.  
 PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.  
 SOURCE: PCT Int. Appl., 285 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RM:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20050119217	A1	20050602	US 2004-975790	20041028 <--
AU 2004284855	A1	20050512	AU 2004-284855	20041029 <--
CA 2542884	A1	20050512	CA 2004-2542884	20041029 <--
EP 1691842	A1	20060823	EP 2004-789807	20041029 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
BR 2004015779	A	20061226	BR 2004-15779	20041029 <--
CN 1901939	A	20070124	CN 2004-80039601	20041029 <--
JP 2007509861	T	20070419	JP 2006-537023	20041029 <--
MX 2006PA04920	A	20070216	MX 2006-PA4920	20060502 <--
IN 2006MN00614	A	20070420	IN 2006-MN614	20060526 <--
NO 2006002420	A	20060731	NO 2006-2420	20060529 <--
PRIORITY APPLN. INFO.:			US 2003-516263P	P 20031030 <--
			WO 2004-CA1900	W 20041029
AB	The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.			
IT	264461-73-6, BAY-43-9006			
RL:	THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with			

chemotherapeutic agent)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)

IC ICM A61K048-00  
ICS A61K031-7088; A61P035-00; A61K031-55  
CC 1-6 (Pharmacology)  
Section cross-reference(s): 3, 14  
IT 199796-52-6, Taxoprexin 200484-11-3, CHS-828 201044-96-4, SB-T-1250  
203258-60-0, Brostallicin 203923-89-1, BNP-1350 204005-46-9, SU5416  
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206873-63-4, Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275  
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492448-75-6, Oncophage 531508-98-2, GCS-100 543726-73-4, IMC-1C11  
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848866-35-3, ER-86526 848866-36-4, AZ10992 848866-48-8, CA 4  
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848873-99-4, SDX-101 848874-01-1, SN-4071 848874-02-2, Urocidin  
849146-37-8, CTP-37 849146-41-4, Pentrix 849146-42-5, ISF-154  
849148-55-6, Norelin 849148-82-9, TransMID-107 849148-97-6, MGV  
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851713-09-2, CDA 11 851713-35-4, 131I-TM 601  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers  
and their use for treatment of proliferative diseases with  
chemotherapeutic agent)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 8 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:346995 HCAPLUS Full-text  
 DOCUMENT NUMBER: 142:411371  
 TITLE: Preparation of pyrimidine derivatives as antitumor agents  
 INVENTOR(S): Dixon, Julie A.; Nagarathnam, Dhanapalan; Zhang, Lei; Wang, Chunguang; Yi, Lin; Chen, Yuanwei; Chen, Jianqing; Bear, Brian; Brands, Michael; Hillisch, Alexander; Bierer, Donald; Wang, Ming; Fu, Wenlang; Hentemann, Martin F.; Bullion, Ann-Marie  
 PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA  
 SOURCE: PCT Int. Appl., 276 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035507	A2	20050421	WO 2004-US33430	20041008 <--
WO 2005035507	A3	20060831		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2542031	A1	20050421	CA 2004-2542031	20041008 <--
EP 1689722	A2	20060816	EP 2004-809919	20041008 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007508321	T	20070405	JP 2006-534438	20041008 <--
US 20050277640	A1	20051215	US 2005-78681	20050310 <--
US 20070117817	A1	20070524	US 2006-573227	20060324 <--
PRIORITY APPLN. INFO.:			US 2003-510804P	P 20031010 <--
			WO 2004-US33430	W 20041008
OTHER SOURCE(S):	MARPAT 142:411371			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [R1 = H, alkyl, cyclopropyl; R2 = alkyl, cyclopropyl, O-alkyl, etc.; R3 = H, halo; M = CH, N; L = carbonyl, O, (un)substituted-alkylenyl, etc.; J and Y independently = (un)substituted-aryl, -heteroaryl; A = halo, CF3, CN, etc.; m = 0-2] and their pharmaceutically acceptable salts, are prepared and disclosed as useful antitumor agents. Thus, e.g., II was prepared by etherification of 4-chloro-picoline with 4-aminophenol followed by amination of 4-chloro-6-phenylpyrimidin-2-amine (preparation given). The



cytotoxic activity of I towards HCT116 cells was evaluated and selected compds. of the invention displayed IC50 values of less than or equal to 500 nM. I should prove useful in the treatment of hyperproliferative disorders.

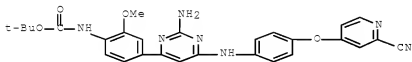
IT 850248-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidine derivs. as antitumor agents)

RN 850248-6-0 HCAPLUS

CN Carbamic acid, [4-[2-amino-6-[4-[(2-cyano-4-pyridinyl)oxy]phenyl]amino]-4-pyrimidinyl]-2-methoxyphenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D239-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT	850246-99-0P	850247-00-6P	850247-01-7P	850247-02-8P	850247-03-9P
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850249-82-0P	850249-83-1P	850249-84-2P	850249-85-3P	850249-86-4P
850249-87-5P	850249-88-6P	850249-89-7P	850249-90-0P	850249-91-1P
850249-92-2P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidine derivs. as antitumor agents)

L110 ANSWER 9 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:283363 HCAPLUS Full-text

DOCUMENT NUMBER: 142:329832

TITLE: Combination of a vegf receptor inhibitor with a chemotherapeutic agent

INVENTOR(S): Bold, Guido; Bruegggen, Josef Bernhard; Huang, Jerry Min-Jian; Kinder, Frederick Ray, Jr.; Lane, Heidi; Latour, Elisabeth Jeanne; Manley, Paul William; Wood, Jeanette Marjorie

PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005027972	A2	20050331	WO 2004-EP10686	20040923 <--
WO 2005027972	A3	20051103		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VC, VN, YU, ZA, ZM, ZW			
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AU 2004273615	A1	20050331	AU 2004-273615	20040923 <--
CA 2537991	A1	20050331	CA 2004-2537991	20040923 <--
EP 1682181	A2	20060726	EP 2004-765542	20040923 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
CN 1856327	A	20061101	CN 2004-80027544	20040923 <--
BR 2004014698	A	20061128	BR 2004-14698	20040923 <--
JP 2007505938	T	20070315	JP 2006-527348	20040923 <--
MX 2006PA03163	A	20060605	MX 2006-PA3163	20060320 <--
IN 2006CN00982	A	20070615	IN 2006-CN982	20060322 <--

NO 2006001777	A	20060623	NO 2006-1777	20060421 <--
US 20080085902	A1	20080410	US 2007-573163	20070228 <--
PRIORITY APPLN. INFO.:			US 2003-505250P	P 20030923 <--
			WO 2004-EP10686	W 20040923

OTHER SOURCE(S): MARPAT 142:329832

AB The present invention relates to a combination therapy for treating patients suffering from proliferative diseases or diseases associated with persistent angiogenesis. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: an aromatase inhibitor; an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist; a topoisomerase I inhibitor or a topoisomerase II inhibitor; a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound; a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: a bradykinin 1 receptor or an angiotensin II antagonist; a cyclooxygenase inhibitor, a bisphosphonate, a heparanase inhibitor (prevents heparan sulfate degradation), e.g., PI-88, a biol. response modifier, preferably a lymphokine or interferons, e.g., interferon  $\gamma$ , an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways; an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor; a telomerase inhibitor, e.g., telomestatin; a protease inhibitor, a matrix metalloproteinase inhibitor, a methionine aminopeptidase inhibitor, e.g., bengamide or a derivative thereof, or a proteasome inhibitor, e.g., PS-341. The patient is treated with: (a) a VEGF inhibitor compound (b) one or more chemotherapeutic agents selected from the group consisting of: agents used in the treatment of hematol. malignancies or FMS-like tyrosine kinase inhibitors; an HSP90 inhibitors; HDAC inhibitors; mTOR inhibitors; somatostatin receptor antagonists; integrin antagonists; anti-leukemic compds.; tumor cell damaging approaches such as ionizing radiation EDG binders; anthranilic acid amide class of kinase inhibitors; ribonucleotide reductase inhibitors; S-adenosylmethionine decarboxylase inhibitors; antibodies against VEGF or VEGFR; photodynamic therapy; angiostatic steroids; implants containing corticosteroids; ATL receptor antagonists; ACE inhibitors.

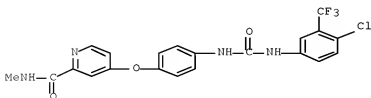
IT 284461-73-0, BAY43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination of vegf receptor inhibitor with chemotherapeutic agent)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K045-06  
ICS A61K031-502

CC 1-6 (Pharmacology)  
 Section cross-reference(s): 63  
 IT 51-21-8, 5-FU 64-86-8D, Colchicine, derivs. 147-94-4, Ara-C  
 12772-57-5, Radicolol 30562-34-6, Geldanamycin 33515-09-2, Gonadorelin  
 40391-99-9, Pamidronic acid 53123-88-9, Rapamycin 75706-12-6, SU101  
 75747-14-7, 17AAG 107868-30-4, Exemestane 112809-51-5, Letrozole  
 118072-93-8, Zoledronic acid 120511-73-1, Anastrozole 120685-11-2,  
 PKC412 127943-53-7, Discodermolide 152459-95-5, Imatinib  
 159351-69-6, RAD 001 162011-90-7, Rofecoxib 162635-04-3, CCI-779  
 169590-42-5, Celecoxib 169944-35-8, Bisulfan 179324-69-7, PS-341  
 180288-69-1, Trastuzumab 181695-72-7, Valdecoxib 184475-35-2,  
 Gefitinib 185077-23-0, PI 88 212141-54-3 212631-79-3, PD184352  
 220064-45-9, GFB 111 220127-57-1, Imatinib mesylate 220991-20-8,  
 Lumiracoxib 252916-29-3, SU6668 260415-63-2, PD173955  
 284461-73-6, BAY43-9006 387867-13-2, MLN518 404950-80-7  
 404951-53-7 572924-54-0, AP 23573  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (combination of vegf receptor inhibitor with chemotherapeutic agent)

L110 ANSWER 10 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:283298 HCAPLUS Full-text

DOCUMENT NUMBER: 142:349042

TITLE: Combinations of chlorpromazine compounds and  
 antiproliferative drugs for the treatment of neoplasms  
 INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen;  
 Keith, Curtis

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916 <--
WO 2005027842	A3	20051222		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004273910	A1	20050331	AU 2004-273910	20040916 <--
CA 2538570	A1	20050331	CA 2004-2538570	20040916 <--
EP 1670477	A2	20060621	EP 2004-788798	20040916 <--
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BR 2004014568	A	20061107	BR 2004-14568	20040916 <--
CN 1878556	A	20061213	CN 2004-80033294	20040916 <--
JP 2007505914	T	20070315	JP 2006-527024	20040916 <--
MX 2006PA03066	A	20060620	MX 2006-PA3066	20060317 <--
NO 2006001325	A	20060606	NO 2006-1325	20060323 <--

KR 2007012618 A 20070126 KR 2006-707244 20060414 <--  
 PRIORITY APPLN. INFO.: US 2003-504310P P 20030918 <--  
 WO 2004-US30368 W 20040916

OTHER SOURCE(S): MARPAT 142:349042

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

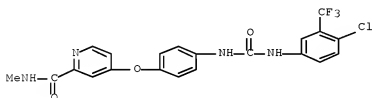
IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chlorpromazine compound-antiproliferative drug antitumor combination)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

IT 189752-49-6, Motexafin 191732-72-6, Revimid 192185-72-1, Tipifarnib 192573-38-9, RPR 109881A 193275-84-2, Lonafarnib 195533-53-0, T 138067 195612-80-7, Galarubicin 196488-72-9, Ranpirnase 199796-52-6, Taxoprexin 200484-11-3, CHS-828 203258-60-0, Brostallicin 203923-89-1, BNP-1350 204005-46-9, SU5416 204205-90-3, D 24851 204318-14-9, Edotreotide 205923-56-4, C225 206873-63-4, Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275 212141-54-3, Vatalanib 213819-48-8, CKD-602 216586-46-8, Virulizin 219923-05-4, ZD 6126 219989-84-1, BMS 247550 220578-59-6 220997-97-7, Diflomotecan 227619-96-7, CP-461 232925-18-7, Thymectacin 246252-04-0, Lutetium texaphyrin 250693-48-2, G 17DT 252916-29-3, SU6668 257933-82-7, EKB-569 257938-36-6, ZD4190 259188-38-0, BMS-275291 263351-82-2, PG-TXL 267243-28-7, Canertinib 284461-73-0, BAY-43-9006 284490-13-7, BCX-1777 292618-32-7, Gimatetan 305838-77-1, Neovastat 337308-14-2, MDX-H 210 339151-96-1, MDX 447 339177-26-3, ABX-EGF 342005-82-7, YM-598 343346-07-6, A 105972 373647-71-3, A 204197 380610-27-5 387867-13-2, MLN518 400010-39-1, SB 408075 414903-37-0, PCK 3145 437755-78-7, GW 2016 439943-59-6, TLK-286 443913-73-3, ZD6474 446022-33-9, AG-2037 492448-75-6, Vitespen 531508-98-2, GCS 100 543726-73-4, IMC 1C11 623174-20-9 634599-18-1 646067-94-9, EKB 509 665026-43-7, CV 247 674289-64-6, AP 5280 824975-76-0, P 54 (pharmaceutical) 848866-30-8, GPX 100 848866-33-1, T 900607 848866-35-3, ER 86526 848866-36-4, AZ 10992 848866-48-8, CA 4 (pharmaceutical) 848866-48-8D, CA 4 (pharmaceutical), prodrug 848871-07-8, CBT 1 848871-42-1, CDC 394 848872-94-6, P 04 848873-95-0, Theralex 848873-96-1, PBI 1402 848873-97-2, SRL 172 848873-98-3, CDA II 848873-99-4, SDX 101 848874-01-1, SN 4071 848874-02-2, Urocidin 848874-03-3, Tyrphostin 1486 849146-37-8, CTP 37 849146-40-3, Synchrovax 849146-41-4, Pentrix 849146-42-5, ISF 154

849148-55-6, Norelin 849148-82-9, TransMID 107 849148-97-6, MGW  
 849149-00-4, GMK (immunomodulator)  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (chlorpromazine compound-antiproliferative drug antitumor combination)

L110 ANSWER 11 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:182644 HCAPLUS Full-text

DOCUMENT NUMBER: 142:280215

TITLE: Preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors

INVENTOR(S): Hoelzemann, Guenter; Ackermann, Karl-August; Staehle, Wolfgang; Jonczyk, Alfred; Rautenberg, Wilfried; Mitjans, Francesc; Rosell-Vives, Elisabet; Adan, Jaume; Soler, Marta; Crassier, Helene

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

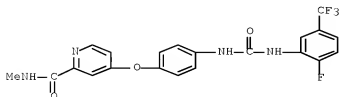
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019192	A1	20050303	WO 2004-EP7224	20040702 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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DE 10334663	A1	20050310	DE 2003-10334663	20030730 <--
AU 2004266781	A1	20050303	AU 2004-266781	20040702 <--
CA 2533963	A1	20050303	CA 2004-2533963	20040702 <--
EP 1651626	A1	20060503	EP 2004-763077	20040702 <--
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JP 2007500136	T	20070111	JP 2006-521413	20040702 <--
US 20060241301	A1	20061026	US 2006-566351	20060130 <--
PRIORITY APPLN. INFO.:			DE 2003-10334663 A	20030730 <--
			WO 2004-EP7224 W	20040702
AB	Twenty-eight title compds. were claimed. Thus, 5-(4-aminophenoxy)benzo-1,2,5-thiadiazole (preparation given), 2-fluoro-5-trifluoromethylphenyl isocyanate, and Et3N were stirred in CH2Cl2 to give 1[4-(benzo-1,2,5-thiadiazol-5-yloxy)phenyl]-3-(2-fluoro-5-trifluoromethylphenyl)urea as the trifluoroacetate. The latter inhibited TIE-2 and RAF kinase with IC50 = 57 nM and 220 nM, resp.			
IT	947054-10-8P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (claimed compound; preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors)			
RN	847054-10-8 HCAPLUS			

CN 2-Pyridinecarboxamide, 4-[4-[[[2-fluoro-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D285-14  
 ICS C07D213-81; C07D213-70; C07D319-18; C07D277-64; C07D307-86;  
 C07D317-64; C07D213-69; C07D235-32; C07D471-04; C07D209-08;  
 A61P035-00; A61K031-435; A61K031-4745; A61K031-4184  
 CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1  
 IT 947054-10-8P 847054-11-9P 847054-12-0P 847054-13-1P  
 847054-14-2P 847054-15-3P 847054-16-4P 847054-18-6P 847054-20-0P  
 847054-22-2P 847054-24-4P 847054-26-6P 847054-28-8P 847054-30-2P  
 847054-31-3P 847054-32-4P 847054-33-5P 847054-34-6P 847054-35-7P  
 847054-36-8P 847054-37-9P 847054-38-0P 847054-39-1P 847054-40-4P  
 847054-41-5P 847054-42-6P 847054-43-7P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (claimed compound; preparation of heteroaryl-substituted diarylureas as  
 tyrosine kinase inhibitors)  
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  
 L110 ANSWER 12 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:141055 HCAPLUS Full-text  
 DOCUMENT NUMBER: 142:240466  
 TITLE: Preparation of piperazinylbenzocycloheptapyridines as  
 farnesyl protein transferase inhibitors useful as  
 antitumor agents.  
 INVENTOR(S): Zhu, Hugh Y.; Cooper, Alan B.; Desai, Jagdish A.;  
 Wang, James J.-S.; Rane, Dinanath F.; Doll, Ronald J.;  
 Njoroge, F. George; Girijavallabhan, Viyyoor M.  
 PATENT ASSIGNEE(S): Schering Corporation, USA  
 SOURCE: PCT Int. Appl., 159 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014577	A1	20050217	WO 2004-US25042	20040804 <--
WO 2005014577	A9	20060323		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				

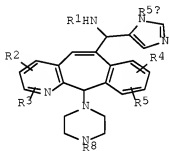
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,  
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

AU 2004263493	A1	20050217	AU 2004-263493	20040804 <--
CA 2535210	A1	20050217	CA 2004-2535210	20040804 <--
US 20050059672	A1	20050317	US 2004-911340	20040804 <--
EP 1660477	A1	20060531	EP 2004-779960	20040804 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004013384	A	20061017	BR 2004-13384	20040804 <--
CN 1863792	A	20061115	CN 2004-80029384	20040804 <--
JP 2007501791	T	20070201	JP 2006-522672	20040804 <--
IN 2006CN00459	A	20070518	IN 2006-CN459	20060203 <--
MX 2006PA01483	A	20060515	MX 2006-PA1483	20060207 <--
NO 2006001077	A	20060505	NO 2006-1077	20060306 <--

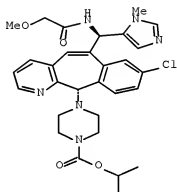
PRIORITY APPLN. INFO.:

US 2003-493269P	P	20030807 <--
US 2003-498509P	P	20030828 <--
WO 2004-US25042	W	20040804

OTHER SOURCE(S): CASREACT 142:240466; MARPAT 142:240466  
 GI



I



II

AB Title compds. [I; R1 = R9X(CR6R7)nCO, R10O2C; n = 1-6; X = O, S, N; R2-R5 = H, Br, Cl, F; R5a = H, alkyl, cycloalkyl; R6, R7 = H, alkyl; R6R7C = C3-7 cycloalkyl; R8 = R11O2C, R11SO2, R12R11aNCO, R21R22R46CO; R9 = alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, etc.; R10 = substituted aryl, heteroaryl, cycloalkyl, alkenyl, alkynyl, etc.; R11 = (substituted) alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl; R11a = H, OH, (substituted) alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, etc.; R12 = H, alkyl, (substituted) piperidinyl, alkylpiperidinyl; R21, R22, R46 = H, alkyl, (substituted) aryl, cycloalkyl, heteroaryl, piperidinyl, etc.], were prepared. Thus, title compound (II) was prepared in several steps from 8-chloro-5,6-dihydro-11H-



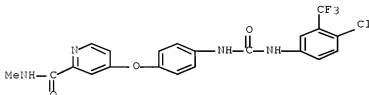
benzo[5,6]cyclohepta[1,2-b]pyridin-11-one. I inhibited FPTase with IC50 in the range of <0.5 nM to 5 nM.

IT 284461-73-0, Bay 43-9006

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-06

ICS C07D401-14; A61K031-415; A61P035-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT 50-35-1, Thalidomide 566-48-3, Formestane 9034-40-6D, Lhrh, analogs  
10540-29-1, Tamoxifen 15663-27-1, Cisplatin 33069-62-4, Taxol  
41575-94-4, Carboplatin 53714-56-0, Leuporelin 65807-02-5, Goserelin  
84449-90-1, Raloxifene 95058-81-4, Gemcitabine 102676-47-1, Fadrozole  
107868-30-4, Exemestane 112809-51-5, Letrozole 114977-28-5, Taxotere  
120511-73-1, Anastrozole 129453-61-8, Fulvestrant 174722-31-7,  
Rituximab 179324-69-7, Bortezomib 180288-69-1, Herceptin  
182167-02-8, Acolbifene 183319-69-9, Osi-774 183321-74-6, Erlotinib  
184475-35-2, Iressa 190977-41-4, Genasense 204005-46-9, Su5416  
205923-56-4, c225 216974-75-3, Bevacizumab 220127-57-1, Gleevec  
284461-73-0, Bay 43-9006 339177-26-3, ABX-EGF 543726-73-4, IMC  
IC11 543726-78-9, SU 6688

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 13 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99470 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:197889

TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for  
treatment of raf, VEGFR, PDGFR, p38 and flt-3  
kinase-mediated diseases

INVENTOR(S): Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm,  
Scott

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

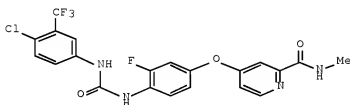
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009961	A2	20050203	WO 2004-US23500	20040722 <--
WO 2005009961	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004259760	A1	20050203	AU 2004-259760	20040722 <--
CA 2532865	A1	20050203	CA 2004-2532865	20040722 <--
US 20050038080	A1	20050217	US 2004-895985	20040722 <--
EP 1663978	A2	20060607	EP 2004-786091	20040722 <--
EP 1663978	B1	20071128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004012219	A	20060822	BR 2004-12219	20040722 <--
CN 1856469	A	20061101	CN 2004-80021091	20040722 <--
JP 2006528196	T	20061214	JP 2006-521221	20040722 <--
ES 2297490	T3	20080501	ES 2004-786091	20040722 <--
MX 2006PA00860	A	20060720	MX 2006-PA860	20060123 <--
IN 2006DN00402	A	20070824	IN 2006-DN402	20060123 <--
NO 2006000870	A	20060407	NO 2006-870	20060222 <--
PRIORITY APPLN. INFO.:				
			US 2003-489102P	P 20030723 <--
			US 2004-540326P	P 20040202
			WO 2004-US23500	W 20040722
OTHER SOURCE(S): CASREACT 142:197889				
GI				



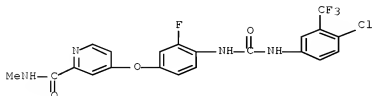
I

- AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.
- IT 735037-03-7P, 4-[[4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid methylamide  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf,  
VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

RN 755037-03-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]-3-fluorophenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT 755037-03-7E, 4-[4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid methylamide  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf,  
VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

IT 835621-07-3P 835621-06-4P 835621-09-5F

835621-10-8P, [4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid amide 835621-11-9P  
835621-12-0F

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf,  
VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

L110 ANSWER 14 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99357 HCAPLUS Full-text

DOCUMENT NUMBER: 142:198088

TITLE: Preparation of pyrimidinecarboxamides,  
pyrimidinylcarbamates and related compounds as  
inhibitors of T cell activation for the treatment of  
inflammatory diseases

INVENTOR(S): Nunes, Joseph J.; Zhu, Xiaotian; Amouzegh, Patricia;  
Ghiron, Chiara; Johnston, David N.; Power, Eoin  
Christopher

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 462 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009443	A1	20050203	WO 2004-US20243	20040624 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20050209221 A1 20050922 US 2004-875896 20040623 <--  
 AU 2004258862 A1 20050203 AU 2004-258862 20040624 <--  
 CA 2529734 A1 20050203 CA 2004-2529734 20040624 <--  
 EP 1648464 A1 20060426 EP 2004-777011 20040624 <--

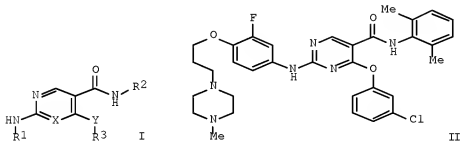
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.:

US 2003-482375P P 20030624 <--  
 US 2004-875896 A 20040623  
 WO 2004-US20243 W 20040624

OTHER SOURCE(S): MARPAT 142:198088

GI

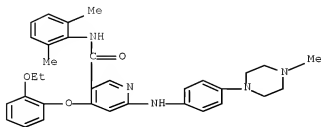


AB Pyrimidine and pyridine carboxamides I [wherein X = N or CH; Y = NH, O or S; R1 - R3 = certain (un)substituted monocyclic or bicyclic ring; or pharmaceutically acceptable salts thereof] as well as pyrimidinylcarbamates were prepared as inhibitors of T cell activation. For example, 2,4-dichloropyrimidine-5-carbonyl chloride, obtained by globally chlorination of uracil-5-carboxylic acid monohydrate with PCl5 in POCl3, underwent amidation with 2,6-dimethylaniline, followed by etherification with 3-chlorophenol and subsequent amination with 3-fluoro-4-(3-(4-methyl-1-piperazinyl)propoxy)aniline to give pyrimidinecarboxamide II. Representative compds. I exhibited inhibition with IC50 values of <10 µM in the LCK-homogeneous time resolved fluorescent kinase assay. Therefore, I and pharmaceutical compns. thereof are useful in the treatment of many diseases such as inflammation.

IT 835641-38-8P, N-(2,6-Dimethylphenyl)-4-[[2-(ethoxy)phenyl]oxy]-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-3-pyridinecarboxamide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (inhibitor; preparation of pyrimidinecarboxamides and pyrimidinylcarbamates as inhibitors of T cell activation for treatment of inflammatory diseases)

RN 835641-38-8 HCAPLUS

CN 3-Pyridinecarboxamide, N-(2,6-dimethylphenyl)-4-(2-ethoxyphenoxy)-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]- (CA INDEX NAME)



IC ICM A61K031-506

ICS A61K031-505; C07D239-46; C07D239-48

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

IT 835641-38-8P, N-(2,6-Dimethylphenyl)-4-[[2-(ethoxy)phenyl]oxy]-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-3-pyridinecarboxamide  
835641-39-9P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-40-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide  
835641-41-3P, 2-[[3,5-Bis(methoxy)-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-42-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-(methoxy)-4-[[2-(4-methyl-1-piperazinyl)ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-43-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-(methoxy)-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-44-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-[(difluoromethyl)oxy]-4-(4-methyl-1-piperazinyl)phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-45-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-chloro-4-(4-(1-methylethyl)-1-piperazinyl)phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-46-8P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methoxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-47-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methoxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-48-0P 835641-49-1P, 4-[[3-(Acetylaminophenyl]oxy]-2-[[4-(diethylamino)butyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-50-4P, 4-[[3-(Acetylaminophenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-51-5P, 4-[[2-Chloro-4-(1-pyrrolidinyl)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-52-6P, 2-[[3,4-Bis(methoxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-53-7P, N-(2,6-Dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]ami

no]-5-pyrimidinecarboxamide 835641-54-8P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-55-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[(4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-56-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl]methyl]oxy]phenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-57-1P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-58-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[3-[(1R)-1-methylpropyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-59-3P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[3-[(1R)-1-methylpropyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-60-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[(4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[3-[(1R)-1-methylpropyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-61-7P 835641-62-8P 835641-63-9P, 4-[[4-[4-(Diethylamino)-4-oxobutyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-64-0P, 4-[[4-[4-(Diethylamino)-4-oxobutyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-65-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(2-pyridinyl)methyl]-5-pyrimidinecarboxamide 835641-66-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(2-pyridinyl)methyl]-5-pyrimidinecarboxamide 835641-67-3P, 2-[[3-Chloro-4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-4-[[2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-68-4P, 2-[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-69-5P, 4-[[2,2-Dimethyl-2,3-dihydrobenzo[b]furan-7-yl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835641-70-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-71-9P, 4-[[2,2-Dimethyl-2,3-dihydrobenzo[b]furan-7-yl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-methyl-3-piperidinyl]methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-72-0P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(1S)-1-phenylethyl]-5-pyrimidinecarboxamide 835641-73-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(1S)-1-phenylethyl]-5-pyrimidinecarboxamide 835641-74-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(4-fluorophenyl)-5-pyrimidinecarboxamide 835641-75-3P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluorophenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-76-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2-fluorophenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2-fluorophenyl)-5-pyrimidinecarboxamide 835641-77-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2-fluorophenyl)-2-[[3-fluoro-4-[[3-

(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835641-78-6P, 4-[[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trimethylphenyl)-5-pyrimidinecarboxamide 835641-79-7P,  
 4-[[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trimethylphenyl)-5-pyrimidinecarboxamide 835641-80-0P, 4-[[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trifluorophenyl)-5-pyrimidinecarboxamide 835641-81-1P, 4-[[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trifluorophenyl)-5-pyrimidinecarboxamide 835641-82-2P, 4-[[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-83-3P, 4-[[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-84-4P, 2-[[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[[4-[2-(diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-85-5P, 4-[[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-86-6P, 4-[[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-87-7P, 4-[[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835641-88-8P,  
 2-[[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[[4-[2-(diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-89-9P,  
 N-(2,6-Dimethylphenyl)-4-[[[2-(methyloxy)-4-[3-oxo-3-(1-pyrrolidinyl)propyl]phenyl]oxy]-2-[[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-90-2P,  
 2-[[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-91-3P,  
 N-(2,6-Dimethylphenyl)-2-[[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-92-4P,  
 N-(2,6-Dimethylphenyl)-2-[[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-93-5P,  
 2-[[[4-[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-94-6P,  
 N-(2,6-Dimethylphenyl)-2-[[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-95-7P,  
 N-(2,6-Dimethylphenyl)-2-[[[3-fluoro-4-[[1-(methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-96-8P,  
 N-(2,6-Dimethylphenyl)-2-[[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-97-9P,  
 4-[[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-98-0P, 4-[[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-

pyrimidinecarboxamide 835641-99-1P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-2-[[4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-00-7P, 2-[[4-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-propylphenyl]oxy]-5-pyrimidinecarboxamide 835642-01-8P, 2-[[3-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-propylphenyl]oxy]-5-pyrimidinecarboxamide 835642-02-9P, 2-[[4-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-03-0P, 2-[[3-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-04-1P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl] (methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-05-2P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-06-3P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-07-4P, 2-[[4-[[[2-(Diethylamino)ethyl] (methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[1-pyrrolidinyl]carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-08-5P, 2-[[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[1-pyrrolidinyl]carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-09-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[1-pyrrolidinyl]carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-10-9P, 2-[[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-11-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-12-1P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-13-2P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-14-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-15-4P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-16-5P, 4-[[2-Chloro-4-[[diethylamino]carbonyl]phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl] (methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-17-6P, 2-[[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[[1-(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-18-7P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[[1-(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-19-8P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[[1-(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-20-1P, N-(2,6-Dimethylphenyl)-4-[[4-[[1-(1-



methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[3-[[3-(1-  
 piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-21-2P, 2-[[4-[[2-(Diethylamino)ethyl](methylethyl)amino]carbonyl]phenyl  
 ]amino]-N-(2,6-dimethylphenyl)-4-[[4-[[1-(methylethyl)amino]carbonyl]-2-  
 (methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-22-3P,  
 N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-  
 piperazinyl]ethyl]oxy]phenyl]amino]-4-[[4-[[1-(methylethyl)amino]carbonyl]-  
 2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-23-4P,  
 N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-(methyl-3-  
 piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[[1-(1-  
 methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-  
 pyrimidinecarboxamide 835642-24-5P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-  
 dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[[1-(1-  
 methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-  
 pyrimidinecarboxamide 835642-25-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-  
 methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-  
 [(cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-  
 dimethylphenyl)-5-pyrimidinecarboxamide 835642-26-7P,  
 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-  
 dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-  
 piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-27-8P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-  
 N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl  
 ]amino]-5-pyrimidinecarboxamide 835642-28-9P, 4-[[4-  
 [(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-  
 dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-  
 pyrimidinecarboxamide 835642-29-0P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-  
 (methyloxy)phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl](methyl)amino]carbon  
 yl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide  
 835642-30-3P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-  
 N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-  
 piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-31-4P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-  
 N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-(methyl-3-  
 piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-32-5P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-  
 N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-  
 fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-33-6P,  
 4-[[4-[[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-  
 dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-  
 pyrimidinecarboxamide 835642-34-7P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-  
 piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-  
 (4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-35-8P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-  
 piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-  
 (1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-36-9P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-  
 piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-  
 piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-37-0P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-  
 piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-  
 [[1-(methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide  
 835642-38-1P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-  
 piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-  
 dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide  
 835642-39-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-  
 piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[[12-  
 (methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-  
 pyrimidinecarboxamide 835642-40-5P, 2-[[4-[[12-  
 (Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-

dimethylphenyl)-4-[[[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-41-6P,  
N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-42-7P, N-(2,6-Dimethylphenyl)-2-[[[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-43-8P, 2-[[[3,4-Bis(methyloxy)-5-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-44-9P,  
4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-45-0P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-46-1P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-2-[[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-47-2P,  
4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-48-3P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-49-4P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-50-7P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-51-8P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-52-9P, 4-[[2-Chloro-4-[[[1-methylethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-53-0P, 4-[[2-Chloro-4-[[[1-methylethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-54-1P, 4-[[2-Chloro-4-[[[1-methylethyl]amino]carbonyl]phenyl]oxy]-2-[[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-55-2P, 2-[[[3,4-Bis(methyloxy)-5-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[[[1-methylethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-56-3P, N-(2,6-Dimethylphenyl)-4-[[2-ethylimidazo[1,2-a]pyridin-8-yl]oxy]-2-[[[3-fluoro-4-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-57-4P, 2-[[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[[3-[3-(diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-58-5P, 2-[[[3,4-Bis(methyloxy)-5-[[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[[3-[3-(diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-59-6P, 4-[[[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-60-9P, 4-[[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[[3-fluoro-4-[[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide

835642-61-0P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-62-1P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-63-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dichloro-4-fluorophenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-64-3P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dichloro-4-fluorophenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-65-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluoro-2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-66-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluoro-2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-67-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(5-methyl-3-isoxazolyl)methyl]-5-pyrimidinecarboxamide 835642-68-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(5-methyl-3-isoxazolyl)methyl]-5-pyrimidinecarboxamide 835642-69-8P, 4-[[2-Chloro-4-[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-70-1P, 4-[[2-Chloro-4-[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-71-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[(diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-72-3P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-73-4P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[4-[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-74-5P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-75-6P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-(methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-76-7P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-77-8P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[1-(methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-78-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-(methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[3-[[1-(methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-79-0P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[3-[[2-(methyloxy)ethyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-80-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[3-[[2-(methyloxy)ethyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-81-4P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[3-[[1-(methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-

pyrimidinecarboxamide 835642-82-5P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-83-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[3-(cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-84-7P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-85-8P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-86-9P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-87-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-88-1P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-89-2P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-90-5P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-91-6P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-92-7P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-93-8P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[1-(methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[1-(pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibitor; preparation of pyrimidinecarboxamides and pyrimidinylcarbamates as inhibitors of T cell activation for treatment of inflammatory diseases)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 15 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99319 HCAPLUS Full-text

DOCUMENT NUMBER: 142:172181

TITLE: Novel targets of protein kinase-inhibiting drugs for novel disease therapies

INVENTOR(S): Biggs, William H., III; Carter, Todd; Fabian, Miles A.; Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiber, Daniel Kelly; Edeen, Phillip

PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009367	A2	20050203	WO 2004-US23325	20040719 <--
WO 2005009367	A3	20050512		

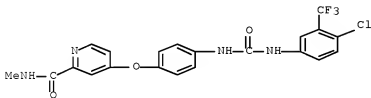
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20060234931      A1      20061019      US 2004-894877      20040719 <--  
 PRIORITY APPLN. INFO.:      US 2003-488513P      P 20030717 <--

AB The invention is directed to the identification and use of addnl. targets of BIRB 796, imatinib mesylate, and BAY 43-9006. The new targets of BIRB 796, imatinib mesylate, and BAY 43-9006 can be used to screen for suitable therapeutic compds. Novel therapeutic and prophylactic uses for BIRB 796, imatinib mesylate, and BAY 43-9006 are disclosed. Protein targets of the drugs were identified using a phage-based competition assay using a panel of 69 proteins including 48 kinases.

IT 284461-73-6, BAY 43-9006  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel targets of protein kinase-inhibiting drugs for novel disease therapies)

RN 284461-73-0 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K  
 CC 7-4 (Enzymes)  
 Section cross-reference(s): 1, 3  
 IT 220127-57-1, Imatinib mesylate 284461-73-0, BAY 43-9006  
 285983-48-4, BIRB 796  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel targets of protein kinase-inhibiting drugs for novel disease therapies)

L110 ANSWER 16 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:55204 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 142:134581

TITLE: Preparation of malonamide derivatives useful as raf-kinase inhibitors

INVENTOR(S): Bruge, David; Buchstaller, Hans-Peter; Wiesner, Matthias; Finsinger, Dirk; Baumgarth, Manfred; Sirrenberg, Christian; Zenke, Frank; Amendt, Christiane; Grell, Matthias

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: PCT Int. Appl., 202 pp.  
CODEN: PIXXD2

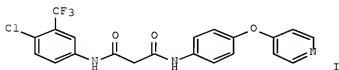
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005389	A2	20050120	WO 2004-EP6573	20040618 <--
WO 2005005389	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004255566	A1	20050120	AU 2004-255566	20040618 <--
CA 2531485	A1	20050120	CA 2004-2531485	20040618 <--
EP 1641759	A2	20060405	EP 2004-740026	20040618 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007508238	T	20070405	JP 2006-518009	20040618 <--
US 20070213374	A1	20070913	US 2007-563830	20070125 <--
PRIORITY APPLN. INFO.:			EP 2003-14556	A 20030707 <--
			WO 2004-EP6573	W 20040618
OTHER SOURCE(S):	MARPAT 142:134581			
GI				



AB Malonamide derivs. of formula A-D-B [wherein: D is (un)substituted bivalent malonamide moiety; A and B are independently selected from (hetero)aryl derivs.], useful as raf-kinase inhibitors (no biol. data), were prepared For instance, malonamide derivative I was obtained via amidation of 3-[(4-chloro-3-trifluoromethylphenyl)amino]-2-oxo-propionic acid by 4-(4-pyridinyloxy)phenylamine with a yield of 57%.

IT 627929-05-0P

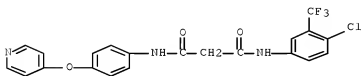
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of malonamide derivs. useful as raf-kinase inhibitors)

RN 827029-05-0 HCAPLUS

CN Propanediamide, N1-[4-chloro-3-(trifluoromethyl)phenyl]-N3-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07D213-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 27, 63

IT 827029-05-0P 827029-06-1P 827029-07-2P 827029-08-3P

827029-09-4P 827029-10-7P 827029-11-8P 827029-22-1P

827029-23-2P 827029-24-3P 827029-25-4P

827029-26-5P 827029-27-6P 827029-28-7P

827029-29-8P 827029-30-1P 827029-31-2P

827029-32-3P 827029-33-4P 827029-34-5P

827029-35-6P 827029-36-7P 827029-37-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(preparation of malonamide derivs. useful as raf-kinase inhibitors)

L110 ANSWER 17 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14200 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:86701

TITLE: Diaryl ureas for treatment of diseases mediated by PDGFR

INVENTOR(S): Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott, William J.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000284	A2	20050106	WO 2004-US15653	20040519 <--
WO 2005000284	A3	20050310		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,			

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG

CA 2526636	A1	20050106	CA 2004-2526636	20040519 <--
US 20050059703	A1	20050317	US 2004-848567	20040519 <--
EP 1626714	A2	20060222	EP 2004-776037	20040519 <--
EP 1626714	B1	20070704		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

JP 2006528986	T	20061228	JP 2006-533210	20040519 <--
AT 366108	T	20070715	AT 2004-776037	20040519 <--
ES 2288694	T3	20080116	ES 2004-776037	20040519 <--
AT 384264	T	20080215	AT 2004-752642	20040519 <--
MX 2005PA12486	A	20060703	MX 2005-PA12486	20051118 <--

PRIORITY APPLN. INFO.:

US 2003-471735P	P	20030520 <--
US 2003-520399P	P	20031117 <--
US 2004-556062P	P	20040325
WO 2004-US15653	W	20040519

OTHER SOURCE(S): MARPAT 142:86701

AB The present invention provides methods for treating and/or preventing conditions and diseases in humans and other mammals that are associated with and/or mediated by signal transduction pathways comprising platelet-derived growth factor receptor (PDGFR), especially PDGFR- $\beta$ , by administering diaryl ureas. The present invention also provides devices and methods for treating, ameliorating, preventing, or modulating restenosis following angioplastic surgery or other invasive procedures that affect or injure the vascular system, and graft rejection following transplantation of a donor tissue into a host, where a stent or other implantable device comprises an effective amount of diaryl ureas. For example, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-fluorophenyl] urea, and N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-chlorophenyl]urea showed an IC50 of less than 10  $\mu$ M in a pPDGFR- $\beta$  sandwich ELISA in A549 cells.

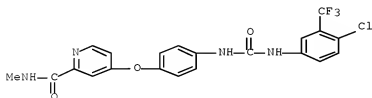
IT 284461-73-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diaryl ureas for prevention and/or treatment of diseases mediated by platelet-derived growth factor receptor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-00

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

IT 57-13-6D, Urea, diaryl derivs. 284461-73-0 284461-74-1

284461-80-9 284462-18-6 284462-19-7



475207-59-1 583840-03-3 583840-04-4

755037-03-7 755037-03-7D, salts 755037-04-8

757229-80-4 819792-84-2 819792-85-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diaryl ureas for prevention and/or treatment of diseases mediated by platelet-derived growth factor receptor)

L110 ANSWER 18 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1313901 HCAPLUS Full-text

DOCUMENT NUMBER: 144:51598

TITLE: Preparation of amino-substituted pyrimidines as antitumor agents

INVENTOR(S): Dixon, Julie A.; Nagarathnam, Dhanapalan; Zhang, Lei; Wang, Chunguang; Yi, Lin; Chen, Yuanwei; Chen, Jianqing; Bear, Brian R.; Brands, Michael; Hillisch, Alexander; Bierer, Donald; Wang, Ming; Fu, Wenlang; Hentemann, Martin F.; Bullion, Ann-Marie; Patel, Manoj

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 182 pp., Cont.-in-part of Appl. No. PCT/US04/033430.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050277640	A1	20051215	US 2005-78681	20050310 <--
WO 2005035507	A2	20050421	WO 2004-US33430	20041008 <--
WO 2005035507	A3	20060831		

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 2003-510804P	P 20031010 <--
	WO 2004-US33430	A2 20041008

OTHER SOURCE(S): CASREACT 144:51598; MARPAT 144:51598

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [R1 = H, alkyl, cyclopropyl; R2 = alkyl, cyclopropyl, O-alkyl, etc.; R3 = H, halo; M = CH, N; L = carbonyl, O, (un)substituted alkylenyl, etc.; J and Y independently = substituted aryl, heteroaryl; A = halo, CF3, CN, etc.; m = 0-2] and their pharmaceutically acceptable salts, are prepared and disclosed as useful antitumor agents. Thus, coupling 6-chloro-N4-(4-[(2-(trifluoromethyl)pyridin-4-yl)oxy]phenyl)pyrimidine-2,4- diamine with 1,3-

dimethylphenylboronic acid afforded 56% II which showed IC50 of 62 nM in test for cytotoxic activity on HCT-116 cells.

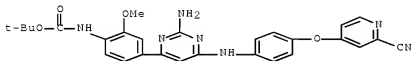
IT 950248-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino-substituted pyrimidines as antitumor agents)

RN 850248-93-0 HCAPLUS

CN Carbamic acid, [4-(2-amino-6-[[4-[(2-cyano-4-pyridinyl)oxy]phenyl]amino]-4-pyrimidinyl]-2-methoxyphenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM A61K031-5377

ICS A61K031-506; C07D413-14; C07D043-02

INCL 514235500; 514252140; 514256000; 544122000; 544295000; 544296000; 544329000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

IT 850246-99-0P	850247-00-6P	850247-01-7P	850247-02-8P	850247-03-9P
850247-04-0P	850247-05-1P	850247-07-3P	850247-08-4P	850247-09-5P
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850249-92-2P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino-substituted pyrimidines as antitumor agents)

L110 ANSWER 19 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:735326 HCAPLUS Full-text

DOCUMENT NUMBER: 143:229730

TITLE: Preparation of tetrahydroisoquinoline derivatives for treating diseases mediated by protein trafficking or chloride channel activity

INVENTOR(S): Pregel, Marko J.; Hirth, Bradford H.; Kane, John L.; Qiao, Shuang; Gregory, Jill; Cuff, Lisa

PATENT ASSIGNEE(S): Genzyme Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 52 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

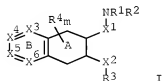
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050176761	A1	20050811	US 2004-6042	20041207 <--
PRIORITY APPLN. INFO.:			US 2003-531873P	P 20031223 <--
OTHER SOURCE(S):			CASREACT 143:229730; MARPAT 143:229730	

GI



AB Tetrahydroisoquinoline derivs. I (variables defined below), pharmaceutical compns. comprising them and methods of treating disease are disclosed herein.

The disclosed compds. are useful in the treatment and prevention of diseases mediated by chloride channel activity and/or protein trafficking, including, but not limited to, diseases associated with impaired mucociliary clearance such as cystic fibrosis, bronchitis, emphysema, and the like. For I the variables are: X1 = CH<sub>2</sub>, CO, SO, SO<sub>2</sub>; X2 = CH<sub>2</sub>, CO, COCH<sub>2</sub>, CO<sub>2</sub>, COS, O, S, SO; X3, X4, X5, X6 = N, CH, wherein at least 1 of X3, X4, X5, X6 = CH; Ring B is optionally substituted in any substitutable carbon; R1 and R2 = H or an optionally substituted aliphatic, aryl, heteroaryl, heterocyclic, cycloalkyl, peptide, or amino acid group, provided that R1 and R2 are not both H; or, R1 and R2, taken together with the nitrogen to which they are bonded, are an optionally substituted heterocyclic group; R3 = optionally substituted aryl, heteroaryl, cycloalkyl, or heterocyclic group; m = 0-2; each R4 = halogen, OH, SH, Ra, ORa, SRa, NH<sub>2</sub>, NHRa, NRa<sub>2</sub>, C(O)NRa<sub>2</sub>, CF<sub>3</sub>, CN, or NO<sub>2</sub>; and Ra = C1-C5 branched or linear alkyl group.

IT 851777-89-4P

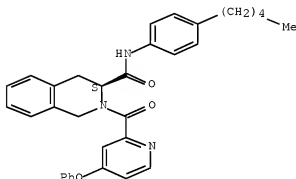
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of tetrahydroisoquinoline derivs. for treating diseases mediated by protein trafficking or chloride channel activity)

RN 851777-89-4 HCAPLUS

CN 3-Isoquinolinecarboxamide, 1,2,3,4-tetrahydro-N-(4-pentylphenyl)-2-[(4-phenoxy-2-pyridinyl)carbonyl]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-4709

ICS A61K031-47

INCL 514310000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 851777-43-0P 851777-46-3P 851777-47-4P 851777-48-5P 851777-49-6P  
 851777-50-9P 851777-52-1P 851777-53-2P 851777-54-3P,  
 2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid  
 N-(4-heptylphenyl)amide 851777-55-4P 851777-56-5P 851777-57-6P  
 851777-59-8P 851777-60-1P 851777-61-2P 851777-62-3P 851777-63-4P,  
 (S)-2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid  
 N-(6-pentylpyridin-3-yl)amide 851777-64-5P 851777-66-7P 851777-67-8P  
 851777-68-9P 851777-69-0P 851777-71-4P 851777-73-6P 851777-76-9P  
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 851777-90-7P 851777-91-8P 851777-92-9P 851777-93-0P,  
 (S)-2-[[5-(Cyclohexyloxy)pyridin-3-yl]carbonyl]-1,2,3,4-

tetrahydroisoquinoline-3-carboxylic acid N-(4-pentylphenyl)amide  
 851777-94-1P 851777-95-2P, (S)-2-(2-isopropoxypropyridine-4-carbonyl)-  
 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (4-pentylphenyl)amide  
 862504-12-9P 862504-13-0P 862504-14-1P 862504-15-2P 862504-16-3P  
 862504-17-4P 862504-18-5P 862504-19-6P 862504-20-9P 862504-21-0P  
 862504-22-1P 862504-23-2P 862504-24-3P, 2-[(Naphthalen-2-yl)carbonyl]-  
 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-(4-chlorophenyl)amide  
 862504-25-4P 862504-26-5P 862504-27-6P 862504-28-7P 862504-29-8P  
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 862504-81-2P 862504-84-5P 862504-87-8P 862504-90-3P 862504-93-6P  
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 tetrahydroisoquinoline-3-carboxylic acid N-(4-pentylphenyl)amide  
 862506-01-2P 862506-10-3P 862506-13-6P, (S)-2-[4-Methoxy-3-[2-  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(drug candidate; preparation of tetrahydroisoquinoline derivs. for treating  
 diseases mediated by protein trafficking or chloride channel activity)

L110 ANSWER 20 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:641861 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 143:146651

TITLE: JAK/STAT inhibitors and MAPK/ERK inhibitors for  
 respiratory syncytial virus (RSV) infection

INVENTOR(S): Mohapatra, Shyam S.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 46 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050159385	A1	20050721	US 2004-18954	20041220 <--
PRIORITY APPLN. INFO.:			US 2003-531052P	P 20031219 <--
AB			The invention discloses a method for treating or reducing the likelihood of developing a RSV infection in a subject by administering an effective amount	

of an inhibitor of the janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling pathway or the mitogen-activated kinase (MAPK)/extracellular signal-regulated kinase (ERK1/2) signaling pathway to the subject. Also disclosed is a pharmaceutical composition that includes an inhibitor of JAK/STAT or MAPK/ERK signaling to the subject; and a pharmaceutically acceptable carrier. Further disclosed is a method for identifying agents useful for treating or reducing the likelihood of developing an RSV infection.

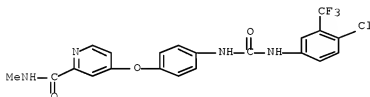
IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus infection treatment)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K048-00

ICS A61K039-395; A61K038-17

INCL 514044000; 514002000; 424146100

CC 1-5 (Pharmacology)

IT 4959-60-8, 4,5-Dimethoxy-2-nitrobenzamide 4998-07-6,  
4,5-Dimethoxy-2-nitrobenzoic acid 21561-09-1 28822-58-4, IBMX  
66575-29-9, Forskolin 109511-58-2, U0126 133550-30-8, AG490  
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4-4'-Hydroxyphenylamino-6,7-dimethoxyquinazoline 210419-07-1, Ro 09-2210  
211555-04-3 212631-79-3, PD184352 220904-83-6, GW5074  
284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus infection treatment)

L110 ANSWER 21 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:469894 HCAPLUS Full-text

DOCUMENT NUMBER: 143:7592

TITLE: Preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors.

INVENTOR(S): Finsinger, Dirk; Buchstaller, Hans-Peter; Burgdorf, Lars; Wiesner, Matthias; Amendt, Christiane; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Ger. Offen., 32 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

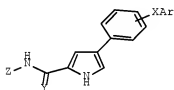
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10354060	A1	20050602	DE 2003-10354060	20031119 <--
AU 2004291255	A1	20050602	AU 2004-291255	20041026 <--
CA 2546334	A1	20050602	CA 2004-2546334	20041026 <--
WO 2005049603	A1	20050602	WO 2004-EP12076	20041026 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1685125	A1	20060802	EP 2004-790859	20041026 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
CN 1882571	A	20061220	CN 2004-80034345	20041026 <--
BR 2004016690	A	20070130	BR 2004-16690	20041026 <--
JP 2007511553	T	20070510	JP 2006-540216	20041026 <--
IN 2006KN00936	A	20070420	IN 2006-KN936	20060417 <--
MX 2006PA05478	A	20060811	MX 2006-PA5478	20060515 <--
US 20070149594	A1	20070628	US 2006-579825	20060517 <--
PRIORITY APPLN. INFO.:			DE 2003-10354060	A 20031119 <--
			WO 2004-EP12076	W 20041026

OTHER SOURCE(S): MARPAT 143:7592

GI



I

AB Title compds. [I; Ar = (substituted) Ph, naphthyl, biphenyl, heterocyclyl; X = O, S, (CH<sub>2</sub>)<sub>n</sub>, CO, (CH<sub>2</sub>)<sub>n</sub>NO, (CH<sub>2</sub>)<sub>n</sub>NH, etc.; n = 1-3; Y = O, S, CHNO<sub>2</sub>, C(CN)<sub>2</sub>, NR<sub>4</sub>; R<sub>4</sub> = H, cyano, OH, etc.; Z = Ar, ArXAr, CH<sub>2</sub>Ar, CH<sub>2</sub>ArXAr; Ar = (substituted) Ph], were prepared as Raf kinase inhibitors (no data). Thus, 4-(PhCH<sub>2</sub>O)C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>H, DMF, and POCl<sub>3</sub> were heated together at 70° for 4 h followed by cooling and addition of ice water and aqueous NaClO<sub>4</sub> to give 98% [2-(4-benzoyloxyphenyl)-3-dimethylaminoallylidene]dimethylammonium perchlorate. This was refluxed 24 h with glycine Et ester hydrochloride in EtOH containing 20% NaOEt to give 91% Et 4-(4-benzoyloxyphenyl)-1H-pyrrole-2- carboxylate. Hydrogenolysis of the latter in EtOAc over Pd/C gave 91% Et 4-(4-hydroxyphenyl)-1H-pyrrole-2-carboxylate. This was heated with 4-chloropyridine-2-carboxylic acid N-methylamide at 160° for 48 h to give 40% Et 4-[4-(2-methylcarbamoylpyridin-4-yloxy)phenyl]-1H-pyrrole-2- carboxylate. Saponification with 2N NaOH in EtOH at 60° for 16 h followed by acidification

with HCl gave 85% free acid, which was stirred 48 h in DMF with 5-amino-2-chlorobenzotrifluoride, N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and 1-hydroxybenzotriazole hydrate to give 17% 4-[4-[5-(4-chloro-3-trifluoromethylphenylcarbamoyl)-1H-pyrrol-3-yl]phenoxy]pyridine-2-carboxylic acid N-methylamide.

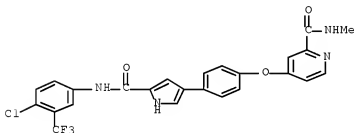
IT 852455-19-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of arylpyrrolicarboxamides as Raf kinase inhibitors for treatment of tumors)

RN 852455-19-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]-1H-pyrrol-3-yl]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-12

ICS A61K031-4439; A61P035-00; A61P017-00; A61P019-00; A61P031-00; A61P013-00; A61P037-00

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 852455-19-7P 852455-20-0P 852455-21-1P

852455-22-2P 852455-23-3P 852455-24-4P

852455-25-5P 852455-26-6P 852455-27-7P

852455-28-8P 852455-29-9P 852455-30-2P

852455-31-3P 852455-32-4P 852455-33-5P

852455-34-6P 852455-35-7P 852455-36-8P

852455-37-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of arylpyrrolicarboxamides as Raf kinase inhibitors for treatment of tumors)

L110 ANSWER 22 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1154653 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:93545

TITLE: Preparation of diaryl ureas with kinase inhibiting activity

INVENTOR(S): Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott, William J.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 122 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

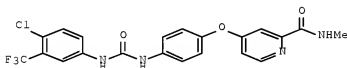
LANGUAGE: English



FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113274	A2	20041229	WO 2004-US15655	20040519 <--
WO 2004113274	A3	20050303		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2526617	A1	20041229	CA 2004-2526617	20040519 <--
US 20050059703	A1	20050317	US 2004-848567	20040519 <--
EP 1636585	A2	20060322	EP 2004-752642	20040519 <--
EP 1636585	B1	20080116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007511203	T	20070510	JP 2006-533211	20040519 <--
AT 366108	T	20070715	AT 2004-776037	20040519 <--
ES 2288694	T3	20080116	ES 2004-776037	20040519 <--
AT 384264	T	20080215	AT 2004-752642	20040519 <--
MX 2005PA12491	A	20060929	MX 2005-PA12491	20051118 <--
US 20070020704	A1	20070125	US 2006-571100	20060728 <--
PRIORITY APPLN. INFO.:				
			US 2003-471735P	P 20030520 <--
			US 2003-520399P	P 20031117 <--
			US 2004-556062P	P 20040325
			WO 2004-US15655	W 20040519

OTHER SOURCE(S): MARPAT 142:93545  
GI



AB Diaryl ureas B-NH-CO-NH-L-(CH<sub>2</sub>)<sub>m</sub>-X-(CH<sub>2</sub>)<sub>p</sub>-L<sub>1</sub>-(Q)<sub>1-3</sub> [I; B = (un)substituted Ph, naphthyl, or heteroaryl; L = (un)substituted Ph, naphthyl, or heteroaryl; X = bond, O, CO, NR<sub>3</sub>, NR<sub>3</sub>CO, S, CONR<sub>3</sub>, CF<sub>2</sub>, CC12, CHF, CH(OH), C.tplbond.C, CH:CH, CR<sub>4</sub>R<sub>5</sub>; m, p = independently 0-4; L<sub>1</sub> = any group L, 5-6 membered cyclic structure; Q = independently COR<sub>4</sub>, CO<sub>2</sub>R<sub>4</sub>, CONR<sub>4</sub>R<sub>5</sub>; each R<sub>3</sub>-R<sub>5</sub> = independently H, (un)substituted C1-5 alkyl, C3-5 cycloalkyl, Ph, C1-3 alkylphenyl, C0-4 alkylheteroaryl], useful to treat diseases and conditions associated with signal transduction pathways comprising of at least one of raf, VEGFR, PDGFR, p38 and/or FLT-3. E.g., a multi-step synthesis of the urea II which produced dose-dependent 45-68% inhibition of tumor growth in a staged HCT 116 colon (mutant k-Ras) xenograft model.

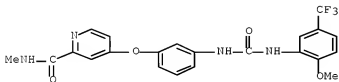
IT 284461-42-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas with kinase inhibiting activity)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07C273-18

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 63

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P  
 284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P  
 284461-42-3P 284461-43-4P 284461-44-5P  
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 284461-73-0P 284461-74-1P 284461-75-2P  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas with kinase inhibiting activity)

L110 ANSWER 23 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:965067 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma

cells, or angiogenesis  
 INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin  
 Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,  
 Jacobus C. A.  
 PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;  
 Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.  
 SOURCE: PCT Int. Appl., 101 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424 <--
WO 2004096224	A3	20041216		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1473043	A1	20041103	EP 2003-9587	20030429 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AU 2004233576	A1	20041111	AU 2004-233576	20040424 <--
CA 2523868	A1	20041111	CA 2004-2523868	20040424 <--
EP 1622619	A2	20060208	EP 2004-729366	20040424 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
BR 2004009919	A	20060425	BR 2004-9919	20040424 <--
JP 2006524634	T	20061102	JP 2006-500099	20040424 <--
MX 2005PA11656	A	20051215	MX 2005-PA11656	20051028 <--
NO 2005005605	A	20051128	NO 2005-5605	20051128 <--
PRIORITY APPLN. INFO.:			EP 2003-9587	A 20030429 <--
			EP 2004-508	A 20040113
			EP 2004-1171	A 20040121
			WO 2004-EP4363	W 20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination preps. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

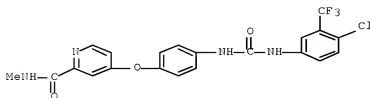
IT 284461-73-6, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine

kinase receptor antagonists and radiotherapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)

IC ICM A61K031-496

ICS A61K031-517; A61P035-00

CC 1-6 (Pharmacology)

Section cross-reference(s): 8, 15

IT 183321-74-6, Erlotinib 183552-38-7, Abarelix 184475-35-2, Gefitinib  
185243-69-0, Etanercept 187724-61-4, PKI-166 190977-41-4, Oblimersen  
191732-72-6, Revimid 204005-46-9, SU-5416 205923-56-4, Cetuximab  
206181-63-7, Ibritumomab 212141-54-3, Vatalanib 213327-37-8,  
Oregovomab 215369-21-4, DC 101 216503-57-0, Alemtuzumab 216503-58-1,  
Mitumomab 216974-75-3, Avastin 252003-65-9, CP-547632 252916-29-3,  
SU-6668 257933-82-7, EKB-569 262367-70-4 263338-11-0 267227-08-7,  
Apolizumab 284461-73-0, BAY-43-9006 288383-20-0 289499-45-2,  
CI-1033 305838-77-1, Neovastat 319460-85-0 334949-28-9 334949-30-3  
334949-31-4 334949-32-5 334949-38-1 334950-47-9 339186-68-4,  
EMD-72000 402857-58-3, CEP-7055 437755-78-7, GW 2016 439081-18-2  
439943-59-6, TLK-286 443913-73-3 444731-52-6, GW 786034 543726-73-4,  
IMC 1C11 591207-53-3, LAQ 824 656247-17-5 660412-20-4 660412-24-8  
660412-26-0 660412-27-1 660412-28-2 660412-29-3 660412-30-6  
660412-31-7 660412-33-9 698387-09-6, HKI 272 790241-27-9  
790241-28-0 790241-29-1 790241-30-4 790241-31-5 790713-23-4, MD  
275 (pharmaceutical) 790713-30-3, BAY 57-9006 790713-36-9, IM 842  
790713-55-2, AZD 6474 790713-57-4, BMY 42355 791073-97-7, 1D09C3  
892553-42-3, Vitaxin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and  
migration or apoptosis or angiogenesis including protein tyrosine  
kinase receptor antagonists and radiotherapy)

L110 ANSWER 24 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:817864 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 141:314164

TITLE: preparation of pyridinyloxyphenylethanediarnide derivs. as  
RAF-kinase inhibitorsINVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Zenke,  
Frank; Amendt, Christiane; Grell, Matthias;  
Sirrenberg, Christian

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 197 pp.

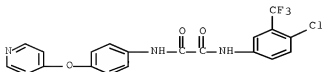
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085399	A1	20041007	WO 2004-EP2406	20040309 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004224239	A1	20041007	AU 2004-224239	20040309 <--
CA 2520009	A1	20041007	CA 2004-2520009	20040309 <--
EP 1606260	A1	20051221	EP 2004-718645	20040309 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
BR 2004007968	A	20060307	BR 2004-7968	20040309 <--
CN 1764645	A	20060426	CN 2004-80007867	20040309 <--
JP 2006521304	T	20060921	JP 2006-504603	20040309 <--
US 20060189665	A1	20060824	US 2005-549852	20050923 <--
PRIORITY APPLN. INFO.:			EP 2003-6702	A 20030324 <--
			WO 2004-EP2406	W 20040309
OTHER SOURCE(S):	CASREACT 141:314164; MARPAT 141:314164			
AB	ADB [D = (substituted) bivalent oxamide moiety; A = L(ML1)a; L = 5-7 membered cyclic structure, preferably aryl, heteroaryl, arylene, heteroarylene; L1 = (substituted) cyclic moiety having at least 5 members, preferably aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group; a = 1-4; L, L1 contain 0-4 N, O, S atoms; B = (substituted) up to tricyclic aryl, heteroaryl containing 0-4 N, O, S atoms], were prepared for treatment of hyperproliferative and nonhyperproliferative disorders (no data). For example, reaction of N-(4-chloro-3- trifluoromethylphenyl)-2-oxoglycine (preparation given) with 4-(4-pyridinyloxy)phenylamine yielded N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]ethanediamine.			
IT 767358-34-9P	RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)			
	(preparation of pyridinyloxyphenylethanediamide derivs. as RAF-kinase inhibitors)			
RN 767358-34-9	HCAPLUS			
CN	Ethanediame, N1-[4-chloro-3-(trifluoromethyl)phenyl]-N2-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)			

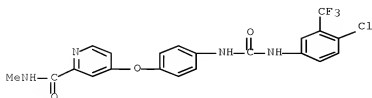


ICS C07D413-12; C07D213-81; A61P031-00; A61K031-4427; A61P017-06  
 CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1, 63  
 IT 767358-34-9P 767358-35-9P 767358-36-1P 767358-37-2P  
 767358-38-3P 767358-39-4P 767358-40-7P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of pyridinyloxyphenylethanedi-amine derivs. as RAF-kinase  
 inhibitors)  
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 25 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:802884 HCAPLUS Full-text  
 DOCUMENT NUMBER: 141:289056  
 TITLE: Medical use of ras antagonists for the treatment of  
 capillary malformation  
 INVENTOR(S): Vikkula, Miikka; Boon, Laurence; Eerola, Iiro  
 PATENT ASSIGNEE(S): Universite Catholique De Louvain, Belg.  
 SOURCE: PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083458	A1	20040930	WO 2003-EP2913	20030320 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2515519	A1	20040930	CA 2003-2515519	20030320 <--
AU 2003214145	A1	20041011	AU 2003-214145	20030320 <--
EP 1604037	A1	20051214	EP 2003-709806	20030320 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 20060141472	A1	20060629	US 2005-546692	20050928 <--
PRIORITY APPLN. INFO.:			WO 2003-EP2913	W 20030320 <--
AB	The invention relates to the field of vascular anomalies and methods for diagnosing and treating them. The invention provides for the causative gene (RAS1) and mutations therein which are useful for diagnosing inherited capillary malformations. The invention further provides RAS1 antagonists for use in treatment of capillary malformations.			
IT 284461-73-0, BAY 43-9006				
RL:	PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Raf protein inhibitor; diagnosis and treatment of vascular anomalies using primers to detect RAS1 gene mutations and ras protein antagonists)			
RN 284461-73-0 HCAPLUS				
CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c				

arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C12Q001-68  
ICS A61K031-00  
CC 1-8 (Pharmacology)  
Section cross-reference(s): 3  
IT 177075-18-2, ISIS 5132 284461-73-0, BAY 43-9006  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(Raf protein inhibitor; diagnosis and treatment of vascular anomalies  
using primers to detect RASAl gene mutations and ras protein  
antagonists)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 26 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2004:756710 HCAPLUS Full-text  
DOCUMENT NUMBER: 141:277628  
TITLE: Preparation of ureidophenoxycyanopyridines as  
anticancer drugs.  
INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen;  
Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma,  
Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei;  
Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu,  
Qingming  
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA  
SOURCE: PCT Int. Appl., 127 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078747	A1	20040916	WO 2004-US6286	20040301 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20040235829	A1	20041125	US 2004-788029	20040227 <--
AU 2004217977	A1	20040916	AU 2004-217977	20040301 <--
CA 2517361	A1	20040916	CA 2004-2517361	20040301 <--

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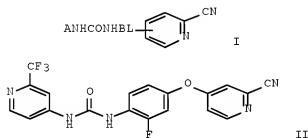
US 20040229937	A1	20041118	US 2004-789446	20040301 <--
US 20050032798	A1	20050210	US 2004-788405	20040301 <--
US 20050038031	A1	20050217	US 2004-788426	20040301 <--
EP 1599467	A1	20051130	EP 2004-716144	20040301 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

BR 2004007897	A	20060301	BR 2004-7897	20040301 <--
JP 2006519264	T	20060824	JP 2006-508977	20040301 <--
CN 1839126	A	20060927	CN 2004-80011547	20040301 <--
IN 2005DN03802	A	20070824	IN 2005-DN3802	20050826 <--

PRIORITY APPLN. INFO.:  
US 2003-450323P P 20030228 <--  
US 2003-450324P P 20030228 <--  
US 2003-450348P P 20030228 <--  
WO 2004-US6286 A 20040301

OTHER SOURCE(S): CASREACT 141:277628; MARPAT 141:277628  
GI

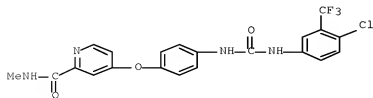


AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxyl, were prepared Thus, 2-trifluoromethyl-4- pyridylamine was stirred 20 h with carbonyldiimidazole in CH2Cl2; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC50 = 7.86 nM to >1600 nM.

IT 284461-73-0, Bay 43-9006  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)





IC ICM C07D401-12  
 ICS C07D405-12; C07D213-79; C07D417-12; A61K031-443; A61K031-444;  
 A61K031-4433; A61K031-4436; A61P035-00  
 CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 27, 63  
 IT 184475-35-2, Iressa 190977-41-4, Oblimersen 191732-72-6, CDC 501  
 192185-72-1, Tipifarnib 193275-84-2, Lonafarnib 195533-53-0, T-138067  
 196488-72-9, Ranpirnase 198153-51-4, Pegasys 199396-76-4, Asoprisnil  
 199796-52-6, Taxoprexin 205923-56-4, Cetuximab 206181-63-7,  
 Ibritumomab tiuxetan 208265-92-3, Neulasta 208921-02-2, Tositumomab  
 209810-58-2, Aranesp 212141-54-3, Vatalanib 215647-85-1, PEG-intron  
 216503-57-0, Campath 216586-46-8, Virulizin 216974-75-3, Avastin  
 219989-84-1, Ixabepilone 220127-57-1, Gleevec 220578-59-6, Gemtuzumab  
 ozogamicin 220581-49-7, Rebif 223378-40-3, Alferon N 263351-82-2,  
 CT-2103 264461-73-6, Bay 43-9006 305838-77-1, Neovastat  
 416841-63-9, Alfaferone 439943-59-6, Tik-286 606967-38-8, MX 6  
 646032-04-4, R 1549 675625-06-6, Affinitak  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coadministration; preparation of ureidophenoxycyanopyridines as anticancer  
 drugs)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 27 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:754414 HCAPLUS Full-text

DOCUMENT NUMBER: 141:277492

TITLE: Preparation of pyridine-containing diaryl ureas useful  
 in the treatment of cancer and other disorders

INVENTOR(S): Dumas, Jacques; Lee, Wendy; Chen, Yuanwei; Adnane,  
 Lila; Scott, William J.; Verma, Sharad; Chen,  
 Jianging; Chen, Zhi; Yi, Lin

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 96 pp.

CODEN: PIIXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

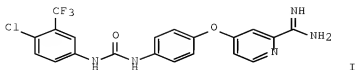
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078128	A2	20040916	WO 2004-US6295	20040301 <--
WO 2004078128	A3	20041223		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
CA 2516627	A1	20040916	CA 2004-2516627	20040301 <--
EP 1603879	A2	20051214	EP 2004-716142	20040301 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
JP 2006519266	T	20060824	JP 2006-508981	20040301 <--
MX 2005PA09102	A	20060531	MX 2005-PA9102	20050826 <--
PRIORITY APPLN. INFO.:			US 2003-450324P	P 20030228 <--
			WO 2004-US6295	W 20040301

OTHER SOURCE(S):  
GI

MARPAT 141:277492



AB The title novel pyridine-containing diaryl ureas ANHC(O)NHBLMQ [A = (un)substituted Ph, naphthyl, heteroaryl, etc.; B = (un)substituted Ph, naphthyl, pyridyl; L = (CH<sub>2</sub>)<sub>m</sub>O(CH<sub>2</sub>)<sub>l</sub>, (CH<sub>2</sub>)<sub>m</sub>(CH<sub>2</sub>)<sub>l</sub>, (CH<sub>2</sub>)<sub>m</sub>C(O)(CH<sub>2</sub>)<sub>l</sub>, etc.; m, l = 0-4; M = (un)substituted pyridine; Q = tetrazolyl, imidazolyl, thiazolyl, etc.], useful for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies, were prepared and formulated. E.g., a multi-step synthesis of I, was given.

IT 758709-43-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

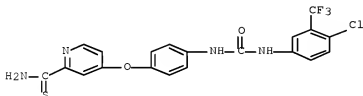
(preparation of pyridine-containing diaryl ureas for treating cancer and

other

disorders)

RN 758709-43-2 HCAPLUS

CN 2-Pyridinecarbothioamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT 758709-43-2P 758709-45-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of pyridine-containing diaryl ureas for treating cancer and

other

disorders)

IT 758709-37-4P 758709-38-5P 758709-40-9P 758709-41-0P  
758709-47-6P 758709-49-8P 758709-51-2P 758709-53-4P  
758709-55-6P 758709-57-8P 758709-59-0P 758709-61-4P  
758709-63-6P 758709-65-6P 758709-67-0P  
758709-69-2P 758709-71-6P 758709-73-8P

758709-75-9P 758709-77-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridine-containing diaryl ureas for treating cancer and

other

disorders)

IT 24484-93-3P 51727-15-2P 73771-11-6P 220000-87-3P  
 228400-44-0P 284462-37-9P 284462-78-8P 573673-43-5P  
 630125-59-8P 757229-80-4P 757230-16-3P 757249-68-6P 757250-67-2P  
 757251-59-5P 757251-60-8P 757251-79-9P 758709-84-1P 758709-88-5P  
 758709-89-6P 758709-90-9P 758709-91-0P 758709-92-1P  
 758709-93-2P 758709-94-3P 758709-95-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridine-containing diaryl ureas for treating cancer and

other

disorders)

L110 ANSWER 28 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:428911 HCAPLUS Full-text

DOCUMENT NUMBER: 141:7028

TITLE: Preparation of 3-substituted-6-aryl pyridines ligands of C5a receptors

INVENTOR(S): Hutchison, Alan; Yuan, Jun; Lee, Kyungae; Maynard, George; Chenard, Bertrand L.; Liu, Nian; Guo, Qin; Guo, Zihong; Hrniciar, Peter

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 366 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

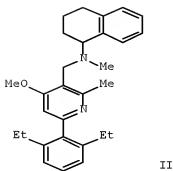
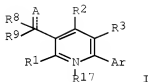
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043925	A2	20040527	WO 2003-US35694	20031107 <--
WO 2004043925	A3	20040805		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2504941	A1	20040527	CA 2003-2504941	20031107 <--
AU 2003291403	A1	20040603	AU 2003-291403	20031107 <--
US 20040158067	A1	20040812	US 2003-704364	20031107 <--
US 7342115	B2	20080311		
EP 1565452	A2	20050824	EP 2003-768799	20031107 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-425281P	P 20021108 <--
			WO 2003-US35694	W 20031107 <--

OTHER SOURCE(S): MARPAT 141:7028

GI



AB The title compds. [I; Ar = (un)substituted Ph, naphthyl, pyridyl, etc.; A = OR4, NR4R5, CR6R7, CHR6R7; R1 = H, halo, NH2, CN, etc.; R2 = halo, CN, XR; R3 = H, halo, OH, etc.; R4 = alkyl, alkenyl, benzoisothiazolyl, etc.; R5 = H, alkyl, alkenyl, etc.; R6 = halo, OH, CN, etc.; R7 = H, halo, OH, etc.; R8 = H, halo, OH, etc.; R9 = absent, H, halo, OH, etc.; X = a bond, O, CO, etc.; R = H, alkyl, alkenyl, etc.; R17 = absent, O] which bind to C5a receptors with high affinity and exhibit neutral antagonist or inverse agonist activity at C5a receptors, and therefore are useful in treating a variety of inflammatory, cardiovascular, and immune system disorders, were prepared and formulated. E.g., a multi-step synthesis of II is given. In addition, the present invention provides labeled 3-substituted-6-aryl pyridines I, which are useful as probes for the localization of C5a receptors.

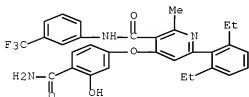
IT 693277-81-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-substituted-6-aryl pyridines as ligands of C5a receptors)

RN 693277-81-5 HCAPLUS

CN 3-Pyridinecarboxamide, 4-[4-(aminocarbonyl)-3-hydroxyphenoxy]-6-(2,6-diethylphenyl)-2-methyl-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT	693276-88-9P	693276-89-0P	693276-90-3P	693276-91-4P	693276-92-5P
	693276-93-6P	693276-94-7P	693276-95-8P	693276-96-9P	693276-97-0P
	693276-98-1P	693276-99-2P	693277-00-8P	693277-01-9P	693277-02-0P

693277-03-1P 693277-04-2P 693277-05-3P 693277-06-4P 693277-07-5P  
 693277-08-6P 693277-09-7P 693277-10-0P 693277-11-1P 693277-12-2P  
 693277-13-3P 693277-14-4P 693277-15-5P 693277-16-6P 693277-17-7P  
 693277-18-8P 693277-19-9P 693277-20-2P 693277-21-3P 693277-22-4P  
 693277-23-5P 693277-24-6P 693277-25-7P 693277-26-8P 693277-27-9P  
 693277-28-0P 693277-29-1P 693277-30-4P 693277-31-5P 693277-32-6P  
 693277-33-7P 693277-34-8P 693277-35-9P 693277-36-0P 693277-37-1P  
 693277-38-2P 693277-39-3P 693277-40-6P 693277-41-7P 693277-42-8P  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of 3-substituted-6-aryl pyridines as ligands of C5a receptors)

L110 ANSWER 29 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:370904 HCAPLUS Full-text

DOCUMENT NUMBER: 140:391200

TITLE: Preparation of pyridinyloxybenzylureas as RAF kinase inhibitors.

INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt, Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg, Christian; Grell, Matthias; Finsinger, Dirk

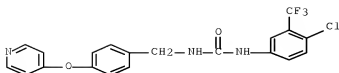
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: PCT Int. Appl., 341 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037789	A2	20040506	WO 2003-EP11134	20031008 <--
WO 2004037789	A3	20041028		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2503445	A1	20040506	CA 2003-2503445	20031008 <--
AU 2003268926	A1	20040513	AU 2003-268926	20031008 <--
EP 1562905	A2	20050817	EP 2003-750697	20031008 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003015580	A	20050830	BR 2003-15580	20031008 <--
CN 1705645	A	20051207	CN 2003-80101925	20031008 <--
JP 2006506454	T	20060223	JP 2005-501513	20031008 <--
MX 2005PA04206	A	20050608	MX 2005-PA4206	20050420 <--
US 20060199844	A1	20060907	US 2005-532574	20050425 <--
ZA 2005004175	A	20060329	ZA 2005-4175	20060117 <--
PRIORITY APPLN. INFO.:			EP 2002-23906	A 20021024 <--
			US 2003-490285P	P 20030728 <--
			WO 2003-EP11134	W 20031008 <--
OTHER SOURCE(S):	MARPAT 140:391200			
AB	ADB [D = methyleneurea moiety or derivative thereof; A = (substituted) L(ML')a; L = 5-7 membered cyclic structure, e.g. aryl, heteroaryl, arylene, heteroarylene; L' = (substituted) cyclic moiety having ≥5 members, e.g. aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group having ≥1 atom; a = 1-4; B = (substituted) up to tricyclic aryl, heteroaryl], were prepared for treatment of hyperproliferative and nonproliferative disorders (no data). Thus, 4-(4-pyridinyloxy)benzylamine (preparation given) and 4-chloro-3- trifluoromethylphenyl isocyanate were stirred together for 2 h in CH2Cl2 to give 1-(4-chloro-3-trifluoromethylphenyl)-3-[4-(4-pyridinyloxy)benzyl]urea.			
IT	685533-65-7P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of methylene urea derivs. as RAF kinase inhibitors)			
RN	685533-65-7 HCAPLUS			
CN	Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[[4-(4-pyridinyloxy)phenyl]methyl]- (CA INDEX NAME)			



IC ICM C07D213-00  
 CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1  
 IT 685533-65-7P 685533-66-8P 685533-67-9P 685533-68-0P  
 685533-69-1P 685533-70-4P 685533-71-5P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of methylene urea derivs. as RAF kinase inhibitors)  
 IT 74-89-5, Methylamine, reactions 76-02-8, Trichloroacetyl chloride  
 98-98-6, Pyridine-2-carboxylic acid 99-93-4, 4-Hydroxyacetophenone  
 108-01-0, 2-Dimethylaminoethanol 109-00-2, 3-Hydroxypyridine 327-78-6,  
 4-Chloro-3-trifluoromethylphenyl isocyanate 367-86-2,  
 4-Fluoro-3-nitrobenzotrifluoride 619-24-9, 3-Nitrobenzonitrile  
 626-55-1, 3-Bromopyridine 767-00-0, 4-Hydroxybenzonitrile 873-62-1,  
 3-Hydroxybenzonitrile 6627-53-8, 5-Chloro-2-nitroanisole 55809-36-4,  
 3-Amino-5-tert-butylisoxazole 56201-88-8 685534-00-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of methylene urea derivs. as RAF kinase inhibitors)

L110 ANSWER 30 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:203667 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 140:253554  
 TITLE: Preparation of pyridinylmethoxyphenylaminoacetamides as  
 RAF kinase inhibitors  
 INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt,  
 Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg,  
 Christian; Grell, Matthias  
 PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany  
 SOURCE: PCT Int. Appl., 182 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019941	A1	20040311	WO 2003-EP8474	20030731 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2496688	A1	20040311	CA 2003-2496688	20030731 <--
AU 2003250197	A1	20040319	AU 2003-250197	20030731 <--

EP 1531817 A1 20050525 EP 2003-790841 20030731 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 CN 1678314 A 20051005 CN 2003-820571 20030731 <--  
 JP 2005539041 T 20051222 JP 2004-531844 20030731 <--  
 US 20060167261 A1 20060727 US 2005-526043 20050228 <--  
 PRIORITY APPLN. INFO.: EP 2002-19023 A 20020827 <--  
 WO 2003-EP8474 W 20030731 <--

OTHER SOURCE(S): MARPAT 140:253554

AB ADB [D = (substituted) bivalent glycinamide moiety; A = L(ML1)a; L = 5-7  
 membered cyclic structure, preferably aryl, heteroaryl, arylene,  
 heteroarylene; L1 = (substituted) cyclic moiety having ≥5 members, preferably  
 aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group;  
 a = 1-4; L, L1 contain 0-4 N, O, S atoms; B = (substituted) up to tricyclic  
 aryl, heteroaryl containing 0-4 N, O, S atoms], were prepared for treatment of  
 hyperproliferative and nonhyperproliferative disorders (no data). Thus, 3-(4-  
 pyridinyloxy)aniline (preparation given), N-(5-tert-butyl-3-isoxazolyl)-2-  
 chloroacetamide (preparation given), and diisopropylethylamine were heated in  
 DMF at 100° for 4 h to give 48% N-(5-tert-butyl-3-isoxazolyl)-2-[3-(4-  
 pyridinyloxy)phenylamino]acetamide.

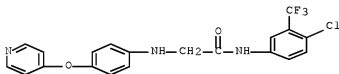
IT 668980-73-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors)

RN 668980-73-2 HCAPLUS

CN Acetamide, N-[4-chloro-3-(trifluoromethyl)phenyl]-2-[[4-(4-  
 pyridinyloxy)phenyl]amino]- (CA INDEX NAME)



IC ICM A61K031-4409

ICS A61K031-4427; C07D213-68; C07D413-12; A61P035-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 27

IT 668980-73-2P 668980-74-3P 668980-75-4P 668980-76-5P

668980-77-6P 668980-78-7P 668980-79-8P 668980-80-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 31 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:533967 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 141:65147

TITLE:  
 Method for treating diseases associated with abnormal  
 tyrosine kinase activity by administering a DNA  
 methylation inhibitor and a tyrosine kinase inhibitor

INVENTOR(S): Lyons, John; Rubinfeld, Joseph

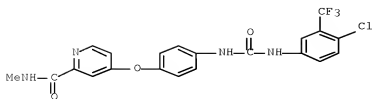


PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S.  
 Ser. No. 71,849.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040127453	A1	20040701	US 2002-206854	20020726 <--
US 6998391	B2	20060214		
US 20030147813	A1	20030807	US 2002-71849	20020207 <--
CA 2474174	A1	20030814	CA 2003-2474174	20030206 <--
WO 2003065995	A2	20030814	WO 2003-US3537	20030206 <--
WO 2003065995	A3	20051013		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003215065	A1	20030902	AU 2003-215065	20030206 <--
EP 1572075	A2	20050914	EP 2003-710881	20030206 <--
EP 1572075	A3	20051207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060140947	A1	20060629	US 2005-181368	20050713 <--
PRIORITY APPLN. INFO.:				
			US 2002-71849	A2 20020207 <--
			US 2002-206854	A 20020726 <--
			WO 2003-US3537	W 20030206 <--

AB Methods are provided for treating diseases associated with abnormal activity of kinases. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT 284461-73-9, BAY 43-9006  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (Raf kinase inhibitor; treating diseases associated with abnormal tyrosine kinase activity by administering DNA methylation inhibitors and tyrosine kinase inhibitors)  
 RN 284461-73-0 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-7072

INCL 514050000

CC 1-12 (Pharmacology)

Section cross-reference(s): 7

IT 284461-73-0, BAY 43-9006

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Raf kinase inhibitor; treating diseases associated with abnormal tyrosine kinase activity by administering DNA methylation inhibitors and tyrosine kinase inhibitors)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 32 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:513393 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 141:71544

TITLE: Preparation of substituted benzazoles as Raf kinase inhibitors

INVENTOR(S): Amiri, Payman; Fantl, Wendy; Levine, Barry Haskell; Poon, Daniel J.; Ramurthy, Savithri; Renhowe, Paul A.; Subramanian, Sharadha; Sung, Leonard

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 476 pp., Cont.-in-part of U.S. Pat. Appl. 2004 87,626.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040122237	A1	20040624	US 2003-675927	20030929 <--
US 20040087626	A1	20040506	US 2003-405945	20030331 <--
US 7071216	B2	20060704		
AU 2004277405	A1	20050414	AU 2004-277405	20040929 <--
CA 2539748	A1	20050414	CA 2004-2539748	20040929 <--
WO 2005032548	A1	20050414	WO 2004-US32161	20040929 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

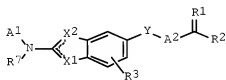
EP 1675584	A1	20060705	EP 2004-789345	20040929 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004014908	A	20061107	BR 2004-14908	20040929 <--
CN 1913884	A	20070214	CN 2004-80032677	20040929 <--
JP 2007507428	T	20070329	JP 2006-528331	20040929 <--
US 20070299039	A1	20071227	US 2005-282939	20051118 <--
MX 2006PA03435	A	20060620	MX 2006-PA3435	20060327 <--
JP 2006193533	A	20060727	JP 2006-96143	20060330 <--
IN 2006KN00838	A	20070413	IN 2006-KN838	20060405 <--

PRIORITY APPLN. INFO.:

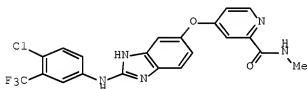
US 2002-369066P	P	20020329 <--
US 2003-405945	A2	20030331 <--
JP 2003-579810	A3	20030331 <--
US 2003-675927	A	20030929 <--
WO 2004-US32161	W	20040929

OTHER SOURCE(S): MARPAT 141:71544

GI



I



II

AB The title compds. I [wherein X1, X2 = N, NR4, O, S (with provisos); Y = O, S; A1 = (un)substituted alkyl, (hetero)cycloalkyl(alkyl), (hetero)aryl(alkyl), etc.; A2 = (un)substituted heteroaryl; R1 = (un) H; R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted (cyclo)alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, heterocyclyl, (hetero)aryl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl; R7 = alkyl; and pharmaceutically acceptable salts, esters, or prodrugs] were prepared as Raf kinase inhibitors. Examples include synthetic methods and phys. data for 1400 compds., as well as descriptions of two Raf kinase bioassays. For instance, 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N-methylcarboxamide were coupled using potassium bis(trimethylsilyl)amide and K2CO3 in DMF to give 4-[(4-amino-3-nitrophenyl)oxy]-N-methylpyridine-2-carboxamide. Pd-catalyzed hydrogenation, followed by cyclization with 4-chloro-3-(trifluoromethyl)benzenesothiocyanate in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide•HCl in THF provided the benzimidazole II. One thousand ninety-four compds. inhibited Raf kinase activity with IC50 < 5 μM in a Raf/Mek filtration assay or a biotinylated Raf screen. Thus, I and

their pharmaceutical compns., which may comprise at least one addnl. agent, are useful for the treatment of Raf kinase mediated disorders, such as cancer (no data).

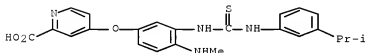
IT 611225-97-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted benzazoles as Raf kinase inhibitors for treatment of cancer)

RN 611225-97-9 HCAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-(methylamino)-3-[[[3-(1-methylethyl)phenyl]amino]thioxomethyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM C07D277-82

ICS C07D263-60

INCL 548161000; 548217000

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT 656-64-4P 823-54-1P 3530-00-5P, 3-Phenoxyphenylisothiocyanate  
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 49559-34-4P 49559-83-3P 54998-08-2P 79110-05-7P 106146-35-4P  
 114780-06-2P 115619-00-6P 115619-01-7P 120381-42-2P 127142-66-9P,  
 (4-Chloro-3-nitrophenyl)isothiocyanate 129488-00-2P 191602-42-3P  
 191602-43-4P, (3-Bromo-4-isopropoxyphenyl)amine 210158-20-6P  
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 [4-Methyl-3-(pyrrolidin-1-yl)phenyl]isothiocyanate 710351-74-9P,  
 4-[[2-[(4-Chloro-3-nitrophenyl)amino]-1-methylbenzimidazol-5-yl]oxy]-N-methylpyridine-2-carboxamide 710351-75-0P, 4-[[2-[(3-Amino-4-chlorophenyl)amino]-1-methylbenzimidazol-5-yl]oxy]-N-methylpyridine-2-

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 710351-82-9P, [3-[2-(Pyrrolidin-1-yl)ethyl]phenyl]amine 710351-83-0P,  
 [3-[2-(Pyrrolidin-1-yl)ethyl]phenyl]isothiocyanate 710351-84-1P,  
 [3-Bromo-4-(2,2,2-trifluoroethoxy)phenyl]amine 710351-85-2P,  
 2-Bromo-4-nitro-1-(2,2,2-trifluoroethoxy)benzene 710351-86-3P,  
 3-Isopropyl-4-fluoroaniline 710351-87-4P, 4-Methyl-3-(3-  
 furyl)nitrobenzene 710351-88-5P, 4-Methyl-3-(3-furyl)aniline  
 710351-89-6P, 4-Methyl-3-(tetrahydrofuran-3-yl)aniline  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (intermediate; preparation of substituted benzazoles as Raf kinase  
 inhibitors for treatment of cancer)

L110 ANSWER 33 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:433797 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:423477

TITLE: Preparation of diaryl ureas as inhibitors of p38  
 kinase

INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques;  
 Khire, Uday; Lowinger, Timothy B.; Scott, William J.;  
 Smith, Roger A.; Wood, Jill E.; Gunn, David E.;  
 Hatoum-Mokdad, Holia; Rodriguez, Marell; Sibley,  
 Robert; Wang, Ming; Turner, Tiffany; Brennan,  
 Catherine

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont. of U.S. Ser. No.  
 458,015, abandoned.  
 CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20040102636	A1	20040527	US 2002-60396	20020201 <--
PRIORITY APPLN. INFO.:			US 1997-126439P	P 19971222 <--
			US 1998-285522	B1 19981222 <--
			US 1999-458015	B1 19991210 <--

OTHER SOURCE(S): MARPAT 140:423477

AB A method of treating a p-38 mediated disease other than cancer comprises  
 administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B =  
 (substituted) aryl, heteroaryl containing  $\geq 1$  6-membered aromatic structure  
 containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-  
 tetrahydrofuran-2-yl)aniline (preparation given) and p-tolyl isocyanate were  
 stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-  
 tetrahydrofuran-2-yl)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited  
 p38 kinase with IC50 = 1-10  $\mu$ M.

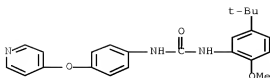
IT 228399-41-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

RN 228399-41-5 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-(4-  
 pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM A61K031-44  
 ICS A61K031-381; A61K031-325; A61K031-277; A61K031-17; A61K031-216;  
 A61K031-195  
 INCL 546306000; 549069000; 558418000; 560024000; 564050000; 564049000;  
 514349000; 514447000; 514485000; 514522000  
 CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1, 27, 28, 63  
 IT 370-50-3P 117745-34-3P 228399-32-4P 228399-33-5P 228399-34-6P  
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of diaryl ureas as inhibitors of p38 kinase)

L110 ANSWER 34 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

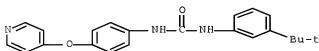
ACCESSION NUMBER: 2004:182368 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:229401

TITLE: Three hybrid assay system for isolating ligand-binding

INVENTOR(S): polypeptides and for isolating small mol. ligands  
Come, Jon H.; Becker, Frank; Kley, Nikolai A.;  
Reichel, Christoph  
PATENT ASSIGNEE(S): Gpc Biotech Inc., USA; Gpc Biotech AG  
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S.  
Ser. No. 91,177.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040043388	A1	20040304	US 2002-234985	20020903 <--
US 7135550	B2	20061114		
US 20030165873	A1	20030904	US 2002-91177	20020304 <--
EP 1832589	A1	20070912	EP 2007-8359	20021015 <--
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR, AL, LT, LV, MK				
US 20040266854	A1	20041230	US 2004-820453	20040407 <--
PRIORITY APPLN. INFO.:			US 2001-272932P	P 20010302 <--
			US 2001-278233P	P 20010323 <--
			US 2001-329437P	P 20011015 <--
			US 2002-91177	A2 20020304 <--
			US 2001-336962P	P 20011203 <--
			WO 2002-US6677	A2 20020304 <--
			US 2002-234985	A2 20020903 <--
			EP 2002-797047	A3 20021015 <--
			WO 2002-US33052	A2 20021015 <--
			US 2003-460921P	P 20030407 <--
			US 2003-531872P	P 20031223 <--
AB	The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Preparation of compds., e.g a methotrexate moiety linked by a polyethylene glycol moiety to dexamethasone, is described.			
IT	228399-50-6D, conjugates RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)			
RN	228399-50-6 HCAPLUS			
CN	Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)			



IC ICM C12Q001-68  
ICS G01N033-53; C07H021-04  
INCL 435006000; X43-5 .71; X53-6 2.31; X53-035.0; X55-265.3; X55-250.0;  
X53-612.3; X54-6 .1; X54-020.0; X53-031.7  
CC 1-1 (Pharmacology)

Section cross-reference(s): 9, 28

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 conjugates 388626-62-8D, conjugates 388626-66-2D, conjugates 388626-68-4D, conjugates 388626-70-8D, conjugates 388626-73-1D,  
 conjugates 388626-75-3D, conjugates 388626-78-6D, conjugates 388626-82-2D, conjugates 388626-84-4D, conjugates 388626-86-6D,  
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 conjugates 388626-99-1D, conjugates 388627-01-8D, conjugates 388627-11-0D, conjugates 388627-13-2D, conjugates 388627-35-8D,  
 conjugates 388627-55-2D, conjugates 388627-57-4D, conjugates 388627-59-6D, conjugates 388627-61-0D, conjugates 388627-76-7D,  
 conjugates 391937-51-2D, conjugates 393590-60-8D, conjugates 413599-62-9D, conjugates 431916-96-0D, conjugates  
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (three hybrid assay system for isolating ligand-binding polypeptides  
 and for isolating small mol. ligands)

L110 ANSWER 35 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:950982 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:16736

TITLE: Preparation of diarylurea derivatives useful for the  
 treatment of protein kinase dependent diseases  
 INVENTOR(S): Floersheimer, Andreas; Furet, Pascal; Manley, Paul  
 William; Bold, Guido; Boss, Eugen; Guagnano, Vito;  
 Vaupel, Andrea

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIIXD2

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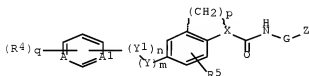
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW  
 RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2484288 A1 20031204 CA 2003-2484288 20030528 <--  
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 AU 2003242591 B2 20070726  
 BR 2003011313 A 20050215 BR 2003-11313 20030528 <--  
 EP 1511730 A2 20050309 EP 2003-755147 20030528 <--  
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 PRIORITY APPLN. INFO.: GB 2002-12413 A 20020529 <--  
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 WO 2003-EP5634 W 20030528 <--

OTHER SOURCE(S): MARPAT 140:16736  
 GI



I

AB The invention relates to the use of diaryl urea derivs. [I; G is not present and Z = a radical of the formula Q; A = CH, N, N→O; A1 = N, N→O, with the proviso that not more than one of A and A1 can be N→O; n = 1, 2; m = 0-2; p = 0, 2, 3; q = 0-5; X = (un)substituted NH if p = 0; or if p is 2 or 3, X = nitrogen which together with (CH2)p and the bonds represented in dotted (interrupted) lines (including the atoms to which they are bound) forms a ring, or X = CHK (wherein K = H or lower alkyl) and p = 0, with the proviso that the bonds represented in dotted lines, if p = 0, are absent; Y1 = O, S, CH2; Y2 = O, S, NH; with the proviso that (Y1)n-(Y2)m does not include O-O, S-S, NH-O, NH-S or S-O groups; R1, R2, R3, R5 = independently H or an inorg. or organic moiety or any two of them together form a lower alkyleneedioxy bridge bound via the oxygen atoms, and the remaining one of these moieties is hydrogen or an inorg. or organic moiety; R4 (if present, i.e., if q is not zero) is an inorg. or organic moiety] or tautomers thereof or pharmaceutically acceptable salts thereof in the treatment of protein kinase dependent diseases or for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, especially a proliferative disease depending on any one or more

of the following (tyrosine) protein kinases such as ras, Abl, VEGF-receptor tyrosine kinase, Flt3, and/or Bcr-Abl activity. Also disclosed are the use of the compds. I for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of the compds. I in the treatment of said diseases, pharmaceutical prepn. comprising the compds. I for the treatment of said diseases, processes for the manufacture of the compds. I, the use or methods of use of the compds. I as mentioned above, and/or the compds. I for use in the treatment of the animal or human body. For example, N-(4-(pyridin-4-yloxy)phenyl)-N'-(4,2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea and N-[4-[6-(4-hydroxyphenylamino)pyrimidin-4-yl]phenyl]-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea at 10  $\mu$ M inhibited gene c-Abl protein kinase by 98%, Kdr receptor tyrosine kinase by 100 and 96%, resp., and Flt3 receptor tyrosine kinase by 100%.

IT 636125-50-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

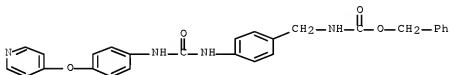
(intermediate; preparation of diarylurea derivs. useful for the treatment

of

protein kinase dependent diseases and proliferative diseases)

RN 630125-50-7 HCAPLUS

CN Carbamic acid, [[4-[[[4-(4-pyridinyloxy)phenyl]amino]carbonyl]amino]phenyl]methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IC ICM C07C275-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 7, 27, 63

IT 393-15-7P, 4-Methoxy-3-trifluoromethylphenylamine 2802-62-2P,  
4,6-Difluoropyrimidine 15862-01-8P, 2-Methoxy-4-nitrobiphenyl  
20566-90-9P, 3-Nitro-N,N-dimethyl-5-trifluoromethylbenzamide  
22227-42-5P, (Piperidin-1-yl) (3-nitro-5-trifluoromethylphenyl)methanone  
56970-24-2P, 2-Methoxybiphenyl-4-ylamine 58609-19-1P 70339-06-9P,  
4-Piperidin-1-yl-3-trifluoromethylphenylamine 102877-78-1P,  
4-(Pyridin-4-yloxy)phenylamine 105130-28-7P, 4-(6-Chloropyrimidin-4-  
yloxy)aniline 105296-03-5P 105298-89-3P 105350-42-3P 118450-89-8P,  
1-(2-Methoxy-4-nitrophenyl)piperidine 124041-03-8P, 4-Chloro-6-(4-  
nitrophenoxy)pyrimidine 168050-39-3P, (4-Aminobenzyl)carbamic acid  
benzyl ester 186090-34-6P 252918-98-2P 260783-12-8P,  
(4-Chloropyridin-2-yl)pyrrolidin-1-ylmethanone 330796-48-0P,  
4-(4-Methylpiperazin-1-yl)-3-trifluoromethylphenylamine 417724-25-5P,  
6-(4-Aminophenoxy)pyrimidin-4-ylamine 630125-30-3P, Methyl[4-(pyridin-4-  
yloxy)phenyl]amine 630125-32-5P, N-(4-Ethylphenyl)-2-(4-  
hydroxyphenyl)acetamide 630125-33-6P 630125-34-7P,  
5-(Pyridin-4-yloxy)-2,3-dihydroindole 630125-35-8P, 6-(Pyridin-4-yloxy)-  
1,2,3,4-tetrahydroquinoline 630125-36-9P, 6-(Pyridin-4-yloxy)quinoline  
630125-37-0P 630125-38-1P, [6-(4-Aminophenoxy)pyrimidin-4-yl][4-(tert-  
butyldimethylsilyloxy)phenyl]amine 630125-39-2P, [4-(tert-  
Butyldimethylsilyloxy)phenyl][6-(4-nitrophenoxy)pyrimidin-4-yl]amine  
630125-40-5P, 4-[6-(4-Nitrophenoxy)pyrimidin-4-ylamino]phenol  
630125-41-6P, 3-Chloro-4-(pyridin-4-yloxy)phenylamine 630125-43-8P,

[6-(4-Aminophenoxy)pyrimidin-4-yl] (4-methoxyphenyl)amine 630125-44-9P,  
 (4-Methoxyphenyl) [6-(4-nitrophenoxy)pyrimidin-4-yl]amine 630125-45-0P  
 630125-46-1P 630125-47-2P 630125-48-3P 630125-50-7P  
 630125-51-8P, [4-(Benzoyloxycarbonylaminomethyl)phenyl]carbamic acid  
 tert-butyl ester 630125-52-9P, 4-(4-Ethylpiperazin-1-yl)-3-  
 methoxyphenylamine 630125-53-0P, 1-Ethyl-4-(2-methoxy-4-  
 nitrophenyl)piperazine 630125-54-1P, 3-Methoxy-4-(piperidin-1-  
 ylmethyl)phenylamine 630125-55-2P, 1-(2-Methoxy-4-nitrobenzyl)piperidine  
 630125-56-3P, (2-Methoxy-4-nitrophenyl)piperidin-1-ylmethanone  
 630125-57-4P, 4-(4-Ethylaminopyrimidin-6-yloxy)aniline 630125-58-5P,  
 4-(4-Aminophenoxy)-2-methoxypyridine 630125-59-6P, 2-Methoxy-4-(4-  
 nitrophenoxy)pyridine 630125-60-9P, 1-Methyl-4-(4-nitrophenoxy)-1H-  
 pyridin-2-one 630125-61-0P, 4-(4-Nitrophenoxy)-1H-pyridin-2-one  
 630125-62-1P, 3-(4-Aminophenoxy)-1H-pyridin-6-one 630125-63-2P,  
 3-(4-Nitrophenoxy)-1H-pyridin-6-one 630125-64-3P, 4-(6-Methoxypyridin-3-  
 ylmethyl)phenylamine 630125-65-4P 630125-66-5P 630125-67-6P,  
 [4-(4-Aminophenoxy)pyridin-2-yl]pyrrolidin-1-ylmethanone  
 630125-68-7P 630125-69-8P, 4-(4-Aminophenoxy)pyridine-2-  
 carbonitrile 630125-70-1P, 4-(2-Chloropyridin-4-yloxy)phenylamine  
 630125-71-2P, 4-(2-Trifluoromethylpyridin-4-yloxy)phenylamine  
 630125-72-3P, 4-(4-Nitrophenoxy)-2-trifluoromethylpyridine 630125-73-4P,  
 4-(6-Fluoropyrimidin-4-yloxy)phenylamine 630125-74-5P,  
 4-(6-Trifluoromethylpyrimidin-4-yloxy)phenylamine 630125-75-6P,  
 [4-(6-Chloropyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester  
 630125-76-7P, 4-(6-Chloropyrimidin-4-ylmethyl)phenylamine 630125-77-8P,  
 [4-(6-Hydroxypyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester  
 630125-78-9P, [4-(6-Hydroxy-2-mercaptopyrimidin-4-ylmethyl)phenyl]carbamic  
 acid tert-butyl ester 630125-79-0P 630125-80-3P, [6-(4-  
 Aminobenzyl)pyrimidin-4-yl]methylamine 630125-81-4P,  
 4-[2-(1H-Tetrazol-5-yl)pyridin-4-yloxy]phenylamine 630125-82-5P,  
 3-Trifluoromethyl-4-(piperidin-1-ylmethyl)phenylamine 630125-83-6P,  
 2,2,2-Trifluoro-N-(4-piperidin-1-ylmethyl-3-trifluoromethylphenyl)acetamid  
 e 630125-84-7P 630125-85-8P 630125-86-9P, 3-Methoxy-4-(4-  
 methylpiperazin-1-ylmethyl)phenylamine 630125-87-0P,  
 3-Methoxy-4-(4-methylpiperazin-1-ylmethyl)nitrobenzene 630125-88-1P,  
 (4-Methylpiperazin-1-yl) (4-nitro-2-methoxyphenyl)methanone 630125-89-2P,  
 3-Trifluoromethyl-5-(piperidin-1-ylmethyl)phenylamine 630125-90-5P  
 630125-91-6P, 3-Trifluoromethyl-4-(4-ethylpiperazin-1-ylmethyl)phenylamine  
 630125-92-7P 630125-93-8P, 3-(4-Ethylpiperazin-1-ylmethyl)-5-  
 trifluoromethylphenylamine 630125-94-9P, (3-Amino-5-  
 trifluoromethylphenyl) (4-ethylpiperazin-1-yl)methanone 630125-95-0P,  
 (3-Nitro-5-trifluoromethylphenyl) (4-ethylpiperazin-1-yl)methanone  
 630125-96-1P, 4-Chloro-6-(4-isocyanatophenoxy)pyrimidine 630125-97-2P  
 630125-98-3P, 3-Amino-N,N-dimethyl-5-trifluoromethylbenzamide  
 630125-99-4P, [6-(4-Aminophenoxy)pyrimidin-4-yl]methylamine  
 630126-00-0P, 3-Pyridin-2-yl-5-trifluoromethylphenylamine 630126-01-1P,  
 Methyl[4-(4-nitrophenoxy)pyrimidin-2-yl]amine 630126-02-2P,  
 2-Chloro-4-(4-nitrophenoxy)pyrimidine 630126-03-3P,  
 4-(2-Methylimidazol-1-yl)-3-trifluoromethylphenylamine 630126-05-5P,  
 2-Methyl-1-(4-nitro-2-trifluoromethylphenyl)-1H-imidazole 630126-07-7P,  
 [6-(4-Amino-2-methylphenoxy)pyrimidin-4-yl]methylamine 630126-09-9P,  
 [3-Methyl-4-(6-methylaminopyrimidin-4-yloxy)phenyl]carbamic acid benzyl  
 ester 630126-11-3P, [4-(6-Chloropyrimidin-4-yloxy)-3-  
 methylphenyl]carbamic acid benzyl ester 630126-12-4P,  
 (4-Hydroxy-3-methylphenyl)carbamic acid benzyl ester 630126-13-5P,  
 6-(4-Aminobenzyl)pyrimidin-4-ylamine 630126-14-6P, [4-(6-Aminopyrimidin-  
 4-ylmethyl)phenyl]carbamic acid tert-butyl ester 630126-15-7P,  
 [4-(6-Azidopyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester  
 630126-16-8P, 5-(6-Chloropyrimidin-4-yloxy)-1H-indole 630126-17-9P,  
 5-(6-Chloropyrimidin-4-yloxy)-2,3-dihydro-1H-indole

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(intermediate; preparation of diarylurea derivs. useful for the treatment

of

protein kinase dependent diseases and proliferative diseases)

IT 228400-22-4P 228400-61-3P 228400-77-9P  
630122-37-1P 630122-38-2P 630122-39-3P  
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630122-68-8P 630122-69-9P 630122-70-2P 630122-71-3P,  
N-[4-(Pyridin-4-yloxy)-3-chlorophenyl]-N'-(3-trifluoromethylphenyl)urea  
630122-72-4P, N-[4-(Pyridin-4-yloxy)-3-methylphenyl]-N'-(3-  
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630122-75-7P 630122-76-8P 630122-77-9P  
630122-78-0P 630122-79-1P 630122-80-4P,  
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[4-(2,2,2-trifluoroethoxy)-3-trifluoromethylphenyl]amide 630122-81-5P  
630122-82-6P 630122-83-7P 630122-84-8P 630122-85-9P  
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630123-15-8P, N-[4-(6-Chloropyrimidin-4-yloxy)phenyl]-N'-(4-chloro-3-  
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N-[4-(6-Chloropyrimidin-4-yloxy)phenyl]-N'-(4-(4-ethylpiperazin-1-yl)-3-  
methoxyphenyl)urea 630123-26-1P, N-[4-(4-Chloropyrimidin-6-yloxy)phenyl]-  
N'-(3-methoxy-4-(piperidin-1-ylmethyl)phenyl)urea 630123-28-3P  
630123-30-7P 630123-32-9P 630123-34-1P 630123-36-3P 630123-38-5P  
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630123-86-3P 630123-87-4P 630123-89-6P, N-[4-(6-Oxo-1,6-dihydropyridin-  
3-ylmethyl)phenyl]-N'-(4-methylphenyl)urea 630123-91-0P 630123-92-1P  
630123-93-2P 630123-94-3P 630123-95-4P 630123-96-5P 630123-97-6P  
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630124-17-3P 630124-18-4P 630124-19-5P 630124-20-8P  
630124-21-9P 630124-22-0P 630124-23-1P  
630124-24-2P 630124-25-3P 630124-26-4P,  
N-[4-(4-Chloropyrimidin-6-yloxy)phenyl]-N'-(3-trifluoromethyl-4-(piperidin-  
1-ylmethyl)phenyl)urea 630124-27-5P, N-[4-(4-Chloropyrimidin-6-

yloxy)phenyl]-N'-[3-methoxy-4-(4-methylpiperazin-1-ylmethyl)phenyl]urea  
 630124-28-6P, N-[4-(4-Azidopyrimidin-6-yloxy)phenyl]-N'-[3-trifluoromethyl-  
 4-(piperidin-1-ylmethyl)phenyl]urea 630124-29-7P 630124-30-0P,  
 N-[4-(4-Chloropyrimidin-6-yloxy)phenyl]-N'-[3-trifluoromethyl-5-(piperidin-  
 1-ylmethyl)phenyl]urea 630124-32-2P, N-[4-(4-Chloropyrimidin-6-  
 yloxy)phenyl]-N'-[3-trifluoromethyl-4-(4-ethylpiperazin-1-  
 ylmethyl)phenyl]urea 630124-34-4P, N-[4-(6-Chloropyrimidin-4-  
 yloxy)phenyl]-N'-[5-trifluoromethyl-3-(4-ethylpiperazin-1-  
 yl)methyl]phenyl]urea 630124-36-6P, N-[4-(6-Chloropyrimidin-4-  
 yloxy)phenyl]-N'-[5-trifluoromethyl-3-(dimethylaminomethyl)phenyl]urea  
 630124-37-7P 630124-38-8P 630124-39-9P 630124-40-2P 630124-42-4P  
 630124-44-6P 630124-46-8P 630124-48-0P 630124-50-4P 630124-52-6P  
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 630124-58-2P 630124-59-3P 630124-60-6P 630124-61-7P 630124-62-8P  
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 630124-68-4P 630124-69-5P 630124-70-8P 630124-71-9P 630124-72-0P  
 630124-73-1P 630124-74-2P 630124-75-3P 630124-77-5P 630124-78-6P  
 630124-80-0P 630124-81-1P 630124-82-2P 630124-84-4P 630124-86-6P  
 630124-88-8P 630124-90-2P 630124-92-4P 630124-94-6P 630124-96-8P  
 630125-16-5P 630125-12-1P 630125-13-2P 630125-15-4P  
 630125-27-8P 630125-28-9P 630125-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of diarylurea derivs. useful for the treatment of protein  
 kinase dependent diseases and proliferative diseases)

L110 ANSWER 36 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:796477 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:307759

TITLE: Preparation of substituted benzazoles as Raf kinase inhibitors

INVENTOR(S): Renhowe, Paul A.; Ramurthy, Savithri; Amiri, Payman; Levine, Barry Haskell; Poon, Daniel J.; Subramanian, Sharadha; Sung, Leonard; Fantl, Wendy

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 259 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

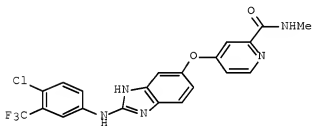
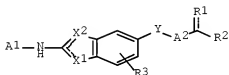
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082272	A1	20031009	WO 2003-US10117	20030331 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2480638	A1	20031009	CA 2003-2480638	20030331 <--
AU 2003226211	A1	20031013	AU 2003-226211	20030331 <--
AU 2003226211	B2	20080529		

EP 1499311 A1 20050126 EP 2003-745683 20030331 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 BR 2003008854 A 20050222 BR 2003-8854 20030331 <--  
 CN 1655779 A 20050817 CN 2003-812193 20030331 <--  
 JP 2005529089 T 20050929 JP 2003-579810 20030331 <--  
 NZ 535985 A 20070427 NZ 2003-535985 20030331 <--  
 IN 2004KN01433 A 20051230 IN 2004-KN1433 20040927 <--  
 MX 2004PA09541 A 20050125 MX 2004-PA9541 20040929 <--  
 NO 2004004617 A 20041228 NO 2004-4617 20041026 <--  
 ZA 2004008386 A 20060531 ZA 2004-8386 20060308 <--  
 JP 2006193533 A 20060727 JP 2006-96143 20060330 <--  
 PRIORITY APPLN. INFO.: US 2002-369066P P 20020329 <--  
 JP 2003-579810 A3 20030331 <--  
 WO 2003-US10117 W 20030331 <--  
 OTHER SOURCE(S): MARPAT 139:307759  
 GI

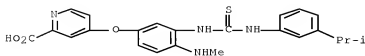


AB The title compds. [I; X1, X2 = N, NR4, O, S (with the provisos); Y = O, S; A1 = (un)substituted alkyl, cycloalkyl, aryl, etc.; A2 = (un)substituted heteroaryl; R1 = O, H, and R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted alkyl, alkoxyalkyl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl], useful for inhibition of Raf kinase activity in a human or animal subject, were prepared E.g., a 3-step synthesis of the benzimidazole II (starting from 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N-methylcarboxamide), was given. The compds. of examples 1-1094 showed a Raf kinase inhibitory activity at an IC50 of less than 5  $\mu$ M. A composition comprising the compound I is claimed. The new compds. compns. may be used either alone or in combination with at least one addnl. agent for the treatment of a Raf kinase mediated disorder, such as cancer.

IT 611225-97-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of substituted benzazoles as Raf kinase inhibitors)

RN 611225-97-9 HCAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-(methylamino)-3-[[[3-(1-methylethyl)phenyl]amino]thioxomethyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K031-41  
 ICS C07D401-12; C07D405-14; C07D409-14; C07D401-14; C07D417-12;  
 C07D417-14; C07D413-14; C07D407-14; C07D413-12; C07D471-08;  
 A61P035-00

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63

IT 823-54-1P 3530-00-5P, 3-Phenoxyphenylisothiocyanate 7748-59-6P  
 7748-60-9P 20734-76-3P 23491-48-7P 49559-34-4P 49559-83-3P  
 54998-08-2P 106146-35-4P 114780-06-2P 115619-00-6P 115619-01-7P  
 120381-42-2P 129488-00-2P 210158-20-6P 211635-75-5P 214337-39-0P  
 219552-64-4P 220000-86-2P 262368-47-8P 284462-57-3P 284462-58-4P  
 401815-98-3P 402948-23-6P 402948-25-8P 402948-26-9P 414880-35-6P  
 483324-01-2P 485841-45-0P 485841-46-1P 485841-47-2P 485841-49-4P  
 611225-42-4P 611225-43-5P 611225-44-6P 611225-45-7P 611225-46-8P  
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 611225-60-6P 611225-61-7P 611225-62-8P 611225-63-9P 611225-64-0P  
 611225-65-1P 611225-66-2P 611225-67-3P 611225-68-4P 611225-69-5P  
 611225-70-8P 611225-71-9P 611225-72-0P 611225-73-1P 611225-74-2P  
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 611225-90-2P 611225-91-3P 611225-92-4P 611225-93-5P 611225-94-6P  
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 611226-15-4P 611226-17-6P 611226-18-7P 611226-19-8P 611226-20-1P  
 611226-21-2P 611226-22-3P 611226-23-4P 611226-24-5P 611226-25-6P  
 611226-26-7P 611226-27-8P 611226-28-9P 611226-29-0P 611226-30-3P  
 611226-31-4P 611226-32-5P 611226-33-6P 611226-34-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of substituted benzazoles as Raf kinase inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 37 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:737931 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 139:255332  
 TITLE: Method for selecting antitumor drug sensitivity-determining factors and method for predicting antitumor drug sensitivity using the selected factors  
 INVENTOR(S): Aoki, Yuko; Hasegawa, Kiyoshi; Ishii, Nobuya; Mori, Kazushige  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 81 pp.  
 CODEN: PIXXD2



DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

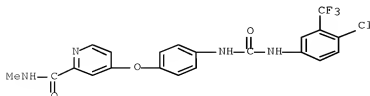
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076660	A1	20030918	WO 2002-JP2354	20020313 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2478640	A1	20030918	CA 2002-2478640	20020313 <--
AU 2002238874	A1	20030922	AU 2002-238874	20020313 <--
EP 1483401	A1	20041208	EP 2002-705127	20020313 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
CN 1625602	A	20050608	CN 2002-828958	20020313 <--
JP 2005519610	T	20050707	JP 2003-574857	20020313 <--
US 20050118600	A1	20050602	US 2005-507389	20050120 <--
PRIORITY APPLN. INFO.:			WO 2002-JP2354	W 20020313 <--

AB Based on drug sensitivity data and extensive gene expression data, a model was constructed by multivariate anal. with the partial least squares method type 1. Further, the model was optimized using modeling power and genetic algorithm. Thereby, the degree of contribution of the resp. genes to drug sensitivity was determined to select genes with a high degree of contribution. In addition, the levels of gene expression in specimens were analyzed, and then the drug sensitivity was predicted based on the model. The predicted values agreed well with those drug sensitivity values determined exptl. The drug sensitivity-predicting method provided by the present invention enables assessment of the effectiveness of a drug prior to administration using small quantities of specimens associated with diseases such as cancer. Since this enables the selection of the most suitable drug for each patient, the present invention is very useful in improving a patient's quality of life (QOL).

IT 284461-73-0, BAY 439006  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C12Q001-68  
ICS G06K009-62; G06F017-17  
CC 1-6 (Pharmacology)  
Section cross-reference(s): 2  
IT 51-21-8, 5-FU 66-22-8, 2,4(1H,3H)-Pyrimidinedione, biological studies  
147-94-4, Ara-C 2207-75-2, Potassium oxonate 2353-33-5, Decitabine  
3094-09-5, Furtulon 4291-63-8, Cladribine 7689-03-4, Camptothecin  
10540-29-1, Tamoxifen 15663-27-1, Cisplatin 17902-23-7, Tegafor  
20830-81-3, Daunomycin 25316-40-9, Adriamycin 33069-62-4, Taxol  
41575-94-4, Carboplatin 53714-56-0, Leuporelin 56420-45-2, Epirubicin  
58957-92-9, Idarubicin 61422-45-5, Carmofur 75607-67-9 82640-04-8,  
LY156758 90357-06-5, ZD 176334 91421-42-0, 9-Nitrocamptothecin  
91421-43-1, 9-Aminocamptothecin 100286-90-6, CPT-11 103766-25-2,  
5-Chloro-2,4-dihydroxypyridine 105149-00-6, TZP4238 107868-30-4,  
FCE24304 110417-88-4, Dolastatin 10 112809-51-5, CGS 20267  
114977-28-5, Taxotere 115767-74-3, TAT59 119804-96-5, DMDC  
120511-73-1, ZD 1033 120685-11-2, CGP41251 123884-00-4, Dolastatin 15  
123948-87-8, Topotecan 126723-15-7, Dolastatin 14 145918-75-8,  
Troxacitabine 149606-27-9, TZT 1027 154361-50-9, Xeloda 159776-69-9,  
Cemadotin 160237-25-2, BMS 184476 169869-90-3, DX-8951f 171179-06-9,  
PD 158780 172481-83-3, BMS 188797 172903-00-3, BBR 3464 182133-25-1,  
LY353381 182167-03-9, EM800 183319-69-9, CP 358774 184475-35-2, ZD  
1839 186348-23-2, IDN 5109 189453-10-9, Epothilone D 192185-68-5,  
R115777 193275-84-2, SCH66336 195987-41-8, BMS 214662 204005-46-9,  
SU5416 212142-18-2, PTK787 212631-79-3, CI1040 219989-84-1, BMS  
247550 220127-57-1, STI-571 220997-97-7, BN-80915 252916-29-3,  
SU6668 253863-00-2, L778123 264461-73-0, BAY 439006  
437755-78-7, GW 2016 443913-73-3, ZD6474 601517-74-2, GW 2286  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(method for selecting antitumor drug sensitivity-determining factors and  
predicting antitumor drug sensitivity using the selected factors)  
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 38 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:656745 HCAPLUS Full-text

DOCUMENT NUMBER: 139:197377

TITLE: Preparation of aryl ureas for therapeutic use as  
kinase inhibitors

INVENTOR(S): Dumas, Jacques; Scott, William J.; Chien, Du-Schieng;  
Lee, Wendy; Bjorge, Susan; Musza, Laszlo L.; Nassar,  
Ala; Riedl, Bernd

PATENT ASSIGNEE(S): Bayer Corporation, USA; Bayer Pharmaceuticals  
Corporation

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

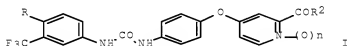
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068746	A1	20030821	WO 2003-US4109	20030211 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,			

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
 UG, US, UZ, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2475818 A1 20030821 CA 2003-2475818 20030211 <--  
 AU 2003209118 A1 20030904 AU 2003-209118 20030211 <--  
 US 20030216446 A1 20031120 US 2003-361859 20030211 <--  
 EP 1474393 A1 20041110 EP 2003-707848 20030211 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 CN 1630638 A 20050622 CN 2003-803705 20030211 <--  
 JP 2005523278 T 20050804 JP 2003-567877 20030211 <--  
 EP 1580188 A1 20050928 EP 2005-7027 20030211 <--  
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 IE, SI, FI, CY, TR, BG, CZ, EE, HU, SK  
 MX 2004PA07830 A 20050701 MX 2004-PA7830 20040811 <--  
 HK 1079774 A1 20071221 HK 2005-111827 20051222 <--  
 PRIORITY APPLN. INFO.: US 2002-354937P P 20020211 <--  
 EP 2003-707848 A3 20030211 <--  
 WO 2003-US4109 W 20030211 <--

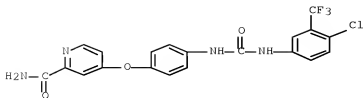
OTHER SOURCE(S): MARPAT 139:197377  
 GI



AB Aryl ureas, such as I [R = Cl, Br; R2 = OH, NH2, NHMe, NHCH2OH, alkoxy; n = 0, 1], were prepared for use in pharmaceutical compns. for the treatment of raf kinase and p38 kinase mediated diseases. These ureas are useful for the treatment of inflammation, osteoporosis, angiogenesis disorders and hyper-proliferative disorders, such as cancer. Thus, urea I (R = Cl, R2 = NHMe, n = 1) was prepared with 57% yield by N-oxidation of I (R = Cl, R2 = NHMe, n = 0) using 3-chloroperbenzoic acid in CH2Cl2 and THF. The prepared ureas were assayed for inhibition of p38 kinase and raf kinase, as well as for cancer cell growth inhibition in human cancer cell lines, such as HCT116 and DLD-1.

IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl(4-pyridyloxy)phenyl)urea  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of aryl ureas for therapeutic use as kinase inhibitors)

RN 284461-74-1 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c-  
 arboxyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM C07D213-79  
ICS C07D213-81; C07D213-89; A61K031-44; A61P011-00; A61P019-00;  
A61P025-00; A61P029-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1, 63

IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-[2-carbamoyl(4-pyridyloxy)phenyl]urea) 284462-18-6P  
583840-03-3P 583840-04-4P 583840-09-9P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

IT 583840-05-5P 583840-06-6P 583840-07-7P  
583840-08-8P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

IT 99586-65-9P, 4-Chloro-2-pyridinecarboxamide 284461-73-0P,  
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-[2-(N-methylcarbamoyl(4-pyridyloxy)phenyl]urea) 284462-80-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 39 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2003:656581 HCAPLUS Full-text  
DOCUMENT NUMBER: 139:197370  
TITLE: Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors  
INVENTOR(S): Dumas, Jacques; Scott, William J.; Riedl, Bernd  
PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: PCT Int. Appl., 67 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

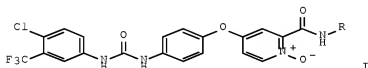
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068229	A1	20030821	WO 2003-US4110	20030211 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003209119	A1 20030904	AU 2003-209119	20030211 <--
US 20030216396	A1 20031120	US 2003-361850	20030211 <--
US 20070265315	A1 20071115	US 2007-775457	20070710 <--
PRIORITY APPLN. INFO.:		US 2002-354935P	P 20020211 <--
		US 2003-361850	B1 20030211 <--
		WO 2003-US4110	W 20030211 <--

OTHER SOURCE(S): MARPAT 139:197370

GI



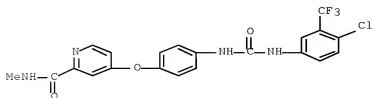
AB The title ureas containing a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH<sub>2</sub>)<sub>m</sub>O(CH<sub>2</sub>)<sub>l</sub>, (CH<sub>2</sub>)<sub>m</sub>(CH<sub>2</sub>)<sub>l</sub>, (CH<sub>2</sub>)<sub>m</sub>CO(CH<sub>2</sub>)<sub>l</sub>, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Preparation of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical composition comprising the title ureas was claimed.

IT 284461-73-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline  
 N-oxide functionality as kinase inhibitors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-44  
 ICS A61K031-47; C07D213-89; C07D215-60; C07D217-08; A61P035-00;  
 A61P029-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1, 63

IT 123-30-8, 4-Aminophenol 320-51-4 176977-85-8, Methyl  
 4-chloro-2-pyridinecarboxylate hydrochloride 284461-73-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline  
 N-oxide functionality as kinase inhibitors)

IT 99586-65-9P 284461-74-1P 284462-80-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline  
 N-oxide functionality as kinase inhibitors)

IT 583840-03-3P 583840-04-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of aryl ureas containing pyridine, quinoline and isoquinoline  
 N-oxide functionality as kinase inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

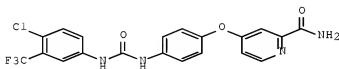
L110 ANSWER 40 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:656580 HCAPLUS Full-text  
 DOCUMENT NUMBER: 139:197369  
 TITLE: Preparation of aryl ureas with angiogenesis inhibiting  
 activity  
 INVENTOR(S): Dumas, Jacques; Scott, William J.; Elting, James;  
 Hatoum-Makdad, Holia  
 PATENT ASSIGNEE(S): Bayer Corporation, USA  
 SOURCE: PCT Int. Appl., 83 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068228	A1	20030821	WO 2003-US4103	20030211 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475703	A1	20030821	CA 2003-2475703	20030211 <--
AU 2003209116	A1	20030904	AU 2003-209116	20030211 <--
US 20030207870	A1	20031106	US 2003-361858	20030211 <--
EP 1478358	A1	20041124	EP 2003-707846	20030211 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005522448	T	20050728	JP 2003-567410	20030211 <--
MX 2004PA07832	A	20050908	MX 2004-PA7832	20040811 <--

10/590724

JP 2007302687  
PRIORITY APPLN. INFO.:

A 20071122

JP 2007-183948  
US 2002-354950P  
JP 2003-567410  
WO 2003-US410320070713 <--  
P 20020211 <--  
A3 20030211 <--  
W 20030211 <--OTHER SOURCE(S): MARPAT 139:197369  
GI

AB The title compds. ANHCONHB [A, B = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, etc.], useful for treating diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Preps. of three title ureas are described. E.g., a 3-step synthesis of the urea I (starting from Me 4-chloro-2-pyridinecarboxylate hydrochloride), was given. The KDR (VEGFR2) assay for testing the title ureas is described.

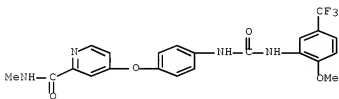
IT 284461-44-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aryl ureas with angiogenesis inhibiting activity)

RN 284461-44-5 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-44

ICS A61K031-4436; A61K031-4725; A61K031-4709; A61K031-17; A61P035-00; A61P017-06; A61P019-02; A61P027-02

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 284461-44-5P 284461-73-0P 284461-74-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aryl ureas with angiogenesis inhibiting activity)

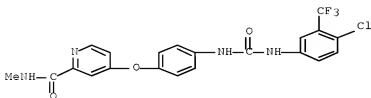
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 41 OF 84 HCAPLUS COPYRIGHT 2008 ACS ON STN  
 ACCESSION NUMBER: 2003:633416 HCAPLUS Full-text  
 DOCUMENT NUMBER: 139:173786  
 TITLE: Method for treating diseases associated with abnormal  
 kinase activity  
 INVENTOR(S): Lyons, John; Rubinfeld, Joseph  
 PATENT ASSIGNEE(S): Supergen, Inc., USA  
 SOURCE: PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003065995	A2	20030814	WO 2003-US3537	20030206 <--
WO 2003065995	A3	20051013		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20030147813	A1	20030807	US 2002-71849	20020207 <--
US 20040127453	A1	20040701	US 2002-206854	20020726 <--
US 6998391	B2	20060214		
CA 2474174	A1	20030814	CA 2003-2474174	20030206 <--
AU 2003215065	A1	20030902	AU 2003-215065	20030206 <--
EP 1572075	A2	20050914	EP 2003-710881	20030206 <--
EP 1572075	A3	20051207		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-71849	A1 20020207 <--
			US 2002-206854	A1 20020726 <--
			WO 2003-US3537	W 20030206 <--
AB	Methods are provided for treating diseases associated with abnormal activity of kinases such as chronic myelogenous leukemia. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor such as imatinib mesylate to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.			
IT	264461-73-6, BAY 43-9006 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of diseases associated with abnormal kinase activity with			



serine/threonine kinase inhibitor and DNA methylation inhibitor)  
 RN 284461-73-0 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K  
 CC 1-6 (Pharmacology)  
 IT 109511-58-2, U0126 154447-36-6, LY294002 167869-21-8, PD98059  
 212631-79-3, PD184352 284461-73-0, BAY 43-9006  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (treatment of diseases associated with abnormal kinase activity with  
 serine/threonine kinase inhibitor and DNA methylation inhibitor)

L110 ANSWER 42 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:454119 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:17567

TITLE: Aryl urea compounds in combination with other  
 cytostatic or cytotoxic agents for treating human  
 cancers and other raf kinase-mediated diseases  
 INVENTOR(S): Carter, Christopher A.; Dumas, Jacques; Gibson, Neil;  
 Hibner, Barbara; Humphrey, Rachel W.; Trail, Pamela;  
 Vincent, Patrick W.; Zhai, Yifan; Riedl, Bernd; Khire,  
 Uday; Lowinger, Timothy B.; Scott, William J.; Smith,  
 Roger A.; Wood, Jill E.; Monahan, Mary-Katherine;  
 Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA; Bayer AG

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

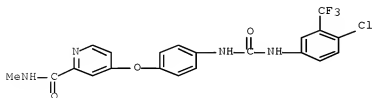
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047579	A1	20030612	WO 2002-US38439	20021203 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

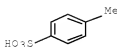
CA 2468463 A1 20030612 CA 2002-2468463 20021203 <--  
 AU 2002351196 A1 20030617 AU 2002-351196 20021203 <--  
 US 20030232765 A1 20031218 US 2002-308187 20021203 <--  
 EP 1450799 A1 20040901 EP 2002-786842 20021203 <--  
 EP 1450799 B1 20061115  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
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 JP 2005511658 T 20050428 JP 2003-548834 20021203 <--  
 AT 345130 T 20061215 AT 2002-786842 20021203 <--  
 EP 1769795 A2 20070404 EP 2006-23696 20021203 <--  
 EP 1769795 A3 20080312  
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 ES 2275931 T3 20070616 ES 2002-786842 20021203 <--  
 RU 2316326 C2 20080210 RU 2004-120785 20021203 <--  
 IN 2004DN01420 A 20070316 IN 2004-DN1420 20040526 <--  
 MX 2004PA05137 A 20050603 MX 2004-PA5137 20040528 <--  
 ZA 2004004225 A 20050829 ZA 2004-4225 20040528 <--  
 US 20060247186 A1 20061102 US 2006-480360 20060705 <--  
 PRIORITY APPLN. INFO.: US 2001-334609P P 20011203 <--  
 EP 2002-786842 A3 20021203 <--  
 US 2002-308187 B1 20021203 <--  
 WO 2002-US38439 W 20021203 <--  
 OTHER SOURCE(S): MARPAT 139:17567  
 AB The invention discloses aryl urea compds. in combination with cytotoxic or  
 cytostatic agents for use in treating raf kinase-mediated diseases, e.g.  
 cancer.  
 IT 475207-59-1  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (aryl urea compds. in combination with other cytostatic or cytotoxic  
 agents for treating human cancers and other raf kinase-mediated  
 diseases)  
 RN 475207-59-1 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA  
 INDEX NAME)  
 CM 1  
 CRN 284461-73-0  
 CMF C21 H16 Cl F3 N4 O3



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



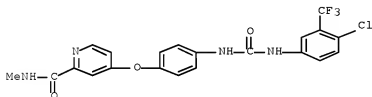
IC ICM A61K031-44  
 ICS A61K031-535; A61K031-65; A61K031-435; A61K031-505; A61K031-47  
 CC 1-6 (Pharmacology)  
 IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-76-0, Actinomycin D 51-21-8, 5-Fluorouracil 57-13-6D, Urea, aryl derivs. 57-22-7, Vincristine 59-05-2, Methotrexate 147-94-4, AraC 148-82-3, Melphalan 154-93-8, BCNU 865-21-4, Vinblastine 4342-03-4, DTIC 5536-17-4, AraA 13010-47-4, CCNU 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 25316-40-9, Doxorubicin hydrochloride 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 71486-22-1, Vinorelbine 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 114977-28-5, Taxotere 122111-03-9, Gemzar 125317-39-7, Navelbine 180288-69-1, Herceptin 184475-35-2, Gefitinib 475207-59-1  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (aryl urea compds. in combination with other cytostatic or cytotoxic agents for treating human cancers and other raf kinase-mediated diseases)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 43 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:454071 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 139:30782  
 TITLE: RAF-MEK-ERK pathway inhibitors to treat cancer  
 INVENTOR(S): Lyons, John F.; Bollag, Gideon  
 PATENT ASSIGNEE(S): Onyx Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 17 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047523	A2	20030612	WO 2002-US38402	20021203 <--
WO 2003047523	A3	20060223		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2466762	A1	20030612	CA 2002-2466762	20021203 <--
AU 2002365899	A1	20030617	AU 2002-365899	20021203 <--

AU 2002365899 B2 20070913  
 US 20030125359 A1 20030703 US 2002-308721 20021203 <--  
 US 7307071 B2 20071211  
 JP 2005526008 T 20050902 JP 2003-548784 20021203 <--  
 EP 1578346 A2 20050928 EP 2002-804478 20021203 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
 PRIORITY APPLN. INFO.: US 2001-336886P P 20011204 <--  
 WO 2002-US38402 W 20021203 <--  
 AB Materials and methods for treating certain cancers are described, preferably  
 cancers that result from the up-regulation of the RAF-MEK-ERK pathway, and  
 more preferably chronic myelogenous leukemia, and which cancer is preferably  
 resistant to the inhibitor of Bcr-Abl tyrosine kinase, imatinib.  
 IT 284461-73-0, BAY 43-9006  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)  
 RN 284461-73-0 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K  
 CC 1-6 (Pharmacology)  
 IT 284461-73-0, BAY 43-9006  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)

L110 ANSWER 44 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:173484 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:221581

TITLE: Method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase

INVENTOR(S): Ayral-kaloustian, Semiramis; Epstein, Joseph William; Birnberg, Gary Harold; Salaski, Edward James; Macewan, Gloria Jean; Cheung, Katherine

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

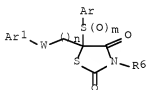
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

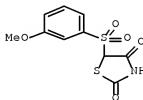
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003018135 A1 20030306 WO 2002-US26691 20020822 <--  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, UZ, VN, YU, ZA, ZM, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG  
AU 2002356135 A1 20030310 AU 2002-356135 20020822 <--  
US 20030144301 A1 20030731 US 2002-226815 20020823 <--  
US 6605628 B2 20030812  
US 20030149063 A1 20030807 US 2002-227084 20020823 <--  
US 6784184 B2 20040831  
PRIORITY APPLN. INFO.: US 2001-314586P P 20010824 <--  
US 2001-314621P P 20010824 <--  
WO 2002-US26691 W 20020822 <--  
OTHER SOURCE(S): MARPAT 138:221581  
GI

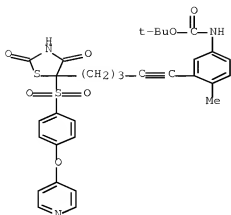


I



II

- AB Title compds. I [Ar = naphthyl, quinolinyl, thienyl, pyridinyl, etc.; m = 0-2; R6 = H, alkyl, benzyl, etc.; W = C.tplbond.C, E/Z-CH=CH, CONH, etc.; n = 1-9; Ar1 = thienyl, pyridinyl, etc.] are prepared For instance, 5-bromothiazolidine-2,4-dione is reacted with 3-methoxybenzenethiol (THF, NaHMDs, -78°-room temperature); the intermediate sulfanyl derivative is oxidized (HOAc, H2O2) to give II. I are inhibitors of Ras FPTase, and may be used as an alternative to, or in conjunction with, traditional cancer therapy for treating ras-oncogene-dependent tumors, such as cancers of the pancreas, colon, bladder, and thyroid.
- IT 500710-93-0P, tert-Butyl [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfonyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase)
- RN 500710-93-0 HCAPLUS
- CN Carbamic acid, [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidinyl]-1-pentynyl]-4-methylphenyl]-, 1,1-dimethylethyl ester (9CI)  
(CA INDEX NAME)



IC ICM A61P035-00  
 CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63  
 IT 125518-56-1P, 5-(4-Fluorophenylsulfonyl)thiazolidine-2,4-dione  
 125540-45-6P 173019-14-2P, 5-[3-(4-Chlorophenyl)-2-propynyl]-5-[(4-methylphenyl)sulfonyl]thiazolidine-2,4-dione 173019-20-0P,  
 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(4-fluorobenzenesulfonyl)thiazolidine-2,4-dione 173019-22-2P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 173019-23-3P, 5-Benzenesulfonyl-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-24-4P,  
 5-Benzenesulfonyl-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-26-6P, 5-(4-Chlorobenzenesulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-27-7P, 5-(4-Chlorobenzenesulfonyl)-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-29-9P,  
 5-(4-Bromobenzenesulfonyl)-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-31-3P, 5-[3-(4-Fluorophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-33-5P,  
 5-(4-Toluenesulfonyl)-5-[3-(p-tolyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-34-6P, 5-(4-Bromobenzenesulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-36-8P, 5-(Naphthalene-2-sulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-38-0P,  
 5-(4-Toluenesulfonyl)-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-40-4P, 5-[3-(4-Methoxyphenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-41-5P,  
 5-[3-(4-Bromophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-43-7P, 5-Benzenesulfonyl-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-45-9P, 5-(4-Chlorobenzenesulfonyl)-5-[3-(4-fluorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-46-0P,  
 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(toluene-3-sulfonyl)thiazolidine-2,4-dione 173019-47-1P, 5-[3-(3-Chlorophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-49-3P,  
 5-Benzenesulfonyl-5-[3-(2-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-51-7P, 5-Benzenesulfonyl-5-[3-[3,5-bis(trifluoromethyl)phenyl]prop-2-ynyl]thiazolidine-2,4-dione 173019-52-8P, 5-[3-[3,5-Bis(trifluoromethyl)phenyl]prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-53-9P, 5-Benzenesulfonyl-5-[3-(3-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-56-2P, 5-(4-Fluorobenzenesulfonyl)-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-62-0P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(quinoline-2-

sulfonyl)thiazolidine-2,4-dione 204848-63-5P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(p-tolylsulfonyl)thiazolidine-2,4-dione 204848-70-4P, 5-[3-(4-Bromophenyl)prop-2-ynyl]-5-(4-chlorobenzenesulfonyl)thiazolidine-2,4-dione 500708-44-1P, 5-(3-Methoxyphenylsulfonyl)thiazolidine-2,4-dione 500708-46-3P, 5-(4-Iodophenylsulfonyl)thiazolidine-2,4-dione 500708-48-5P, 5-((4-(Trifluoromethoxy)benzene)sulfonyl)thiazolidine-2,4-dione 500708-49-6P, 5-(3-Nitrobenzenesulfonyl)thiazolidine-2,4-dione 500708-54-3P, 5-(4-Nitrobenzenesulfonyl)thiazolidine-2,4-dione 500708-60-1P, 5-[[4-(Pyridin-4-yl)oxy]benzene]sulfonyl)thiazolidine-2,4-dione 500708-65-6P, 5-(4-Phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500708-67-8P, 5-(4-Benzyloxybenzenesulfonyl)thiazolidine-2,4-dione 500708-70-3P, 5-(3,4-Dimethoxybenzenesulfonyl)thiazolidine-2,4-dione 500708-73-6P, N-[5-((2,4-Dioxothiazolidine-5-yl)sulfonyl)-2-methoxyphenyl]acetamide 500708-78-1P, 5-(5-Chlorothiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-81-6P, 5-(Thiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-85-0P, 5-(5-(Pyridin-2-yl)thiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-93-0P, 5-(4-Butoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-00-2P 500709-82-0P, 5-(4-Methoxyphenylsulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500709-83-1P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-fluorophenylsulfonyl)thiazolidine-2,4-dione 500709-85-3P, 5-[6-(4-Chlorophenyl)hexan-5-ynyl]-5-(4-methoxyphenylsulfonyl)thiazolidine-2,4-dione 500709-86-4P, 5-[11-(4-Chlorophenyl)undecan-10-ynyl]-5-(4-methoxyphenylsulfonyl)thiazolidine-2,4-dione 500709-87-5P, 5-[5-(2-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-88-6P, 5-[5-(3-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-90-0P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500709-91-1P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-fluorobenzenesulfonyl)thiazolidine-2,4-dione 500709-92-2P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-93-3P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 500709-94-4P, N-[4-[[5-(5-(4-Chlorophenyl)pentan-4-ynyl)-2,4-dioxothiazolidine-5-yl]sulfonyl]phenyl]acetamide 500709-95-5P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(quinoline-8-sulfonyl)thiazolidine-2,4-dione 500709-96-6P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-nitrobenzenesulfonyl)thiazolidine-2,4-dione 500709-97-7P, 5-(4-Benzyloxybenzenesulfonyl)-5-[5-(4-chlorophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500709-98-8P, 5-(4-Butoxybenzenesulfonyl)-5-[5-(4-chlorophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500709-99-9P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(naphthalene-1-sulfonyl)thiazolidine-2,4-dione 500710-01-0P, 5-[5-(2,5-Dichlorophenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-02-1P 500710-03-2P, 5-[5-(2,4-Dichlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-05-4P, 5-[5-(3-Nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-06-5P, 5-(4-Iodobenzenesulfonyl)-5-[5-(4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-07-6P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-08-7P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(2-methyl-5-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-09-8P 500710-10-1P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-11-2P, 5-(4-Iodobenzenesulfonyl)-5-[5-(2-methyl-5-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-12-3P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(naphthalene-1-sulfonyl)thiazolidine-2,4-dione 500710-13-4P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 500710-14-5P, 5-[5-(2-Methyl-4-nitrophenyl)pentan-4-ynyl]-5-[4-(pyridin-4-

yl)oxy)benzene]sulfonyl]thiazolidine-2,4-dione 500710-15-6P,  
5-[5-(2-Methyl-4-nitrophenyl)pentan-4-ynyl]-5-(4-  
phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-16-7P,  
5-(4-Methoxybenzenesulfonyl)-5-[5-(2-methyl-4-nitrophenyl)pentan-4-  
ynyl]thiazolidine-2,4-dione 500710-17-8P, 5-(4-Iodobenzenesulfonyl)-5-[5-  
(2-methyl-4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione  
500710-18-9P 500710-19-0P, 5-[5-(3-Fluoro-5-nitrophenyl)pentan-4-ynyl]-5-  
(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-20-3P,  
5-[5-(2,5-Dimethylphenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-21-4P, 5-[5-(2,5-Dimethylphenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-22-5P,  
5-[5-(2,4-Dimethylphenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-23-6P, 5-[5-(2,4-Dimethylphenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-24-7P  
500710-25-8P, 5-[5-(5-Chloro-2-methylphenyl)pentan-4-ynyl]-5-((4-trifluoromethoxybenzene)sulfonyl)thiazolidine-2,4-dione 500710-26-9P  
500710-27-0P 500710-28-1P 500710-29-2P 500710-30-5P,  
5-[5-(4-Bromo-2-methylphenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-31-6P,  
[4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]phenyl]carbamic acid tert-Butyl Ester 500710-32-7P 500710-33-8P,  
N-tert-Butyl-3-[5-[5-(4-iodobenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylbenzamide 500710-34-9P, [3-[5-[5-(4-iodobenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid tert-Butyl Ester 500710-35-0P,  
[4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-methylphenyl]carbamic acid tert-Butyl Ester 500710-37-2P,  
[4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-trifluoromethylphenyl]carbamic acid tert-Butyl Ester 500710-38-3P  
500710-39-4P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-trifluoromethylphenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-40-7P,  
5-(4-Methoxybenzenesulfonyl)-5-[5-(4-trifluoromethoxyphenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-41-8P, 3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylbenzoic Acid Methyl Ester 500710-42-9P, 5-[5-(4-tert-butylphenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-43-0P, 5-[5-(4-tert-Butylphenyl)pentan-4-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-44-1P,  
4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]benzonitrile 500710-45-2P, 5-[5-(4-(Methanesulfonyl)phenyl)pentan-4-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-47-4P,  
5-(4-Methoxybenzenesulfonyl)-5-[5-(4-(pyrrol-1-yl)phenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-48-5P, 5-(4-Iodobenzenesulfonyl)-5-[5-(4-(pyrrol-1-yl)phenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-49-6P, 5-[5-(4-(Pyrrol-1-yl)phenyl)pentan-4-ynyl]-5-((4-trifluoromethoxybenzene)sulfonyl)thiazolidine-2,4-dione 500710-50-9P,  
5-(3-Methoxybenzenesulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-51-0P, 5-(4-Methylphenylsulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-52-1P,  
5-(4-Methoxybenzenesulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-53-2P, 5-(4-Methoxybenzenesulfonyl)-5-(3-(pyridin-3-yl)prop-2-ynyl)thiazolidine-2,4-dione 500710-54-3P,  
5-(3-(Thiophen-2-yl)prop-2-ynyl)-5-(toluene-4-sulfonyl)thiazolidine-2,4-dione 500710-55-4P, 5-(3-(1,1'-Biphenyl-4-yl)prop-2-ynyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-56-5P,  
5-[3-(4-Phenoxyphenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-57-6P, 5-(3-(1,1'-Biphenyl-4-yl)prop-2-ynyl)-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-59-8P,  
5-(5-(Pyridin-3-yl)pentan-4-ynyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-60-1P, 5-[5-(5-Amino-2-methylphenyl)pentan-4-ynyl]-5-(4-



methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-61-2P,  
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Benzyl Ester 500710-62-3P 500710-63-4P,  
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid 4-chlorophenyl Ester 500710-64-5P,  
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Methyl Ester 500710-65-6P,  
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid isopropyl Ester 500710-66-7P,  
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Neopentyl Ester 500710-67-8P,  
 [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Butyl Ester 500710-68-9P 500710-69-0P,  
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2-methylpropanamide 500710-70-3P,  
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-3,3-dimethylbutanamide 500710-71-4P,  
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2,2-dimethylpropanamide 500710-72-5P,  
 N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2-phenylacetamide 500710-73-6P,  
 N-Benzyl-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-74-7P, N-(4-Methoxyphenyl)-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-75-8P, N-(4-Chlorophenyl)-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-76-9P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-N'-(4-methylphenyl)urea 500710-77-0P, 4-Chloro-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-78-1P, 4-Methoxy-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-79-2P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl][1,1'-biphenyl]-4-carboxamide 500710-80-5P,  
 4-(tert-Butyl)-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-81-6P,  
 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[(5-chloro-2-thienyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-82-7P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-(2-thienylsulfonyl)-1,3-thiazolidine-2,4-dione 500710-83-8P,  
 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[(3,4-dimethoxyphenyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-84-9P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-85-0P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-86-1P,  
 5-[(5-Chloro-2-thienyl)sulfonyl]-5-[5-(2,5-dichlorophenyl)-4-pentynyl]-1,3-thiazolidine-2,4-dione 500710-87-2P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-(2-thienylsulfonyl)-1,3-thiazolidine-2,4-dione 500710-88-3P,  
 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-[(3,4-dimethoxyphenyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-89-4P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-90-7P, [3-[5-[5-[(5-Chloro-2-thienyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamic acid tert-butyl ester 500710-91-8P, tert-Butyl [3-[5-[2,4-dioxo-5-(2-thienylsulfonyl)-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-92-9P, tert-Butyl [3-[5-[5-[(3,4-dimethoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-93-0P, tert-Butyl [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-94-1P, tert-Butyl [3-[5-[2,4-dioxo-5-[[5-

(2-pyridinyl)-2-thienyl)sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-95-2P, N-(tert-Butyl)-3-[5-[5-[(5-chloro-2-thienyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-96-3P, N-(tert-Butyl)-3-[5-[2,4-dioxo-5-(2-thienyl)sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-97-4P, N-(tert-Butyl)-3-(5-[5-[(3,4-dimethoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-98-5P, N-(tert-Butyl)-3-[5-[2,4-dioxo-5-[5-(2-pyridinyl)-2-thienyl)sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-99-6P, 4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-methylbenzoic Acid 500711-00-2P, N-(4-Chlorobenzyl)-3-[5-(4-methoxyphenyl)sulfonyl]-2,4-dioxothiazolidin-5-yl]propionamide 500711-02-4P, N-[2-(4-Chlorophenyl)ethyl]-3-[5-(4-methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]propionamide 500711-03-5P, 5-[(4-[2,4-dioxo-5-(4-Chlorophenyl)pent-4-enyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-08-0P, 5-[3-(4-Chlorophenyl)propyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-09-1P, 5-[5-(3-Aminophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-10-4P, 5-(3-Phenylprop-2-enyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-11-5P 500711-12-6P 500711-13-7P, 5-(4-Methoxyphenyl)sulfinyl]thiazolidine-2,4-dione 500711-14-8P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxyphenyl)sulfinyl]thiazolidine-2,4-dione 500711-15-9P, Benzyl 5-[5-[5-[(benzyloxy)carbonyl]amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-16-0P, 4-Nitrobenzyl 5-[(4-methoxyphenyl)sulfonyl]-5-[5-[2-methyl-5-[[[(4-nitrobenzyl)oxy]carbonyl]amino]phenyl]pentan-4-ynyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-17-1P, Methyl 5-[5-[5-[(methoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-18-2P, Isopropyl 5-[5-[5-[(isopropoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-19-3P 500711-20-6P, Butyl 5-[5-[5-[(butoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-21-7P, Isobutyl 5-[5-[5-[(isobutoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-22-8P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-3-(3-(imidazol-1-yl)propyl)-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-24-0P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)-3-methylthiazolidine-2,4-dione 500711-25-1P, 3-(2,4-Diethoxybenzyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-26-2P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-3-(2,4-diethoxybenzyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-28-4P, 5-[5-(2,5-Dichlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)-2,4-dioxothiazolidine-3-carboxylic acid 2-methoxyethyl ester 500711-31-9P, 5-[3-[3,5-Bis(trifluoromethyl)phenyl]prop-2-ynyl]thiazolidine-2,4-dione 500711-32-0P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pentan-1-ynyl]-4-methylphenyl]carbamic acid neopentyl ester 500711-33-1P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]methyl]phenyl]-N'-(4-methylphenyl)urea  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfonyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



C1

IC ICM C07D417-02  
 ICS C07D413-02; C07D043-02; C07D041-02; A61K031-541; A61K031-5377;  
 A61K031-496; A61K031-4545; A61K031-454; A61K031-427

INCL 514227800; 514235500; 514252130; 514252140; 514253010; 514254010;  
 514316000; 514326000; 514365000; 514397000

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 7, 27

IT 349-65-5P, 2-Methoxy-5-(trifluoromethyl)aniline 703-12-8P,  
 N-Methyl-4-bromobenzenesulfonamide 883-62-5P, 3-Methoxy-2-naphthoic Acid  
 1215-98-1P, 4-(4-Acetylphenoxy)aniline 13041-60-6P, Methyl  
 3-methoxy-2-naphthoate 16588-75-3P, 2-Methoxy-5-(trifluoromethyl)phenyl  
 isocyanate 27237-21-4P, 4-(3-Carboxyphenoxy)-1-nitrobenzene  
 36089-89-1P, 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene 41513-02-4P,  
 4-Bromo-3-(trifluoromethyl)phenyl Isocyanate 50727-06-5P,  
 5-Hydroxyisoindoline-1,3-dione 51727-15-2P, 4-Chloropyridine-2-carbonyl  
 chloride hydrochloride 53750-66-6P, 4-Chloropyridine-2-carbonyl chloride  
 54579-63-4P, 4-(3-Carboxyphenoxy)aniline 64064-63-7P,  
 4-(2-Methyl-5-pyridyloxy)-1-nitrobenzene 67291-63-8P,  
 2-Amino-3-methoxynaphthalene 71708-64-0P, 4-[3-(N-  
 Methylcarbamoyl)phenoxy]-1-nitrobenzene 73441-73-3P,  
 4-[4-(N-Methylsulfamoyl)phenoxy]-1-nitrobenzene 73441-86-8P,  
 4-[4-(N-Methylsulfamoyl)phenyloxy]aniline 75919-92-5P,  
 4-(4-Acetylphenoxy)-1-nitrobenzene 77992-50-8P, 4-Bromo-3-  
 (trifluoromethyl)aniline monohydrochloride 99586-65-9P,  
 4-Chloro-2-pyridinecarboxamide 114780-06-2P, 4-Chloro-N,N-dimethyl-2-  
 pyridinecarboxamide 119431-22-0P, 3-Chloro-4-(2,2,2-  
 trifluoroacetamino)phenol 153435-79-1P, N-Methyl-3-  
 bromobenzenesulfonamide 176977-85-8P, Methyl 4-chloropyridine-2-  
 carboxylate hydrochloride 220000-87-3P, 4-Chloro-N-methyl-2-  
 pyridinecarboxamide 228401-15-8P, 2-[N-(Carbomethoxyloxy)amino]-3-  
 methoxynaphthalene 228401-43-2P, 4-(3-Methoxycarbonyl-4-methoxyphenoxy)-  
 1-nitrobenzene 228401-44-3P, 4-(3-Carboxy-4-methoxyphenoxy)-1-  
 nitrobenzene 284461-86-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-  
 [2-(methoxycarbonyl)-5-pyridyloxy]phenyl]urea 284462-06-2P,  
 N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[2-(2-  
 triisopropylsilyloxyethyl)carbamoyl]-4-pyridyloxy]phenyl]urea  
 284462-37-9P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]aniline 284462-38-0P,  
 5-(4-Nitrophenoxy)isoindoline-1,3-dione 284462-39-1P,  
 5-(4-Aminophenoxy)isoindoline-1,3-dione 284462-40-4P,  
 1-(4-tert-Butyl-2-nitrophenyl)-2,5-dimethylpyrrole 284462-41-5P,  
 5-tert-Butyl-2-(2,5-dimethylpyrrolyl)aniline 284462-42-6P,  
 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-methylaniline hydrochloride  
 284462-43-7P 284462-44-8P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-  
 chloroaniline 284462-45-9P, 4-Chloro-2-methoxy-5-  
 (trifluoromethyl)aniline 284462-46-0P, 4-[3-(N-Methylcarbamoyl)-4-  
 methoxyphenoxy]-1-nitrobenzene 284462-47-1P, 4-[3-(N-Methylcarbamoyl)-4-  
 methoxyphenoxy]aniline 284462-48-2P, 5-(4-Nitrophenoxy)-2-  
 methylisoindoline-1,3-dione 284462-49-3P, 5-(4-Aminophenoxy)-2-  
 methylisoindoline-1,3-dione 284462-51-7P, 4-Chloro-2-[N-(2-morpholin-4-  
 ylethyl)carbamoyl]pyridine 284462-52-8P, 4-[2-[N-(2-Morpholin-4-

ylethyl)carbamoyl]-4-pyridyloxy]aniline 284462-53-9P,  
 4-(1-Oxoisoindolin-5-yloxy)-1-nitrobenzene 284462-54-0P,  
 4-(1-Oxoisoindolin-5-yloxy)aniline 284462-55-1P, 4-(3-Ethoxycarbonylphenoxy)-1-nitrobenzene 284462-56-2P, 4-[3-(N-Methylcarbamoyl)phenoxy]aniline 284462-57-3P, 4-(5-Methoxycarbonyl-3-pyridyloxy)-1-nitrobenzene 284462-58-4P, 4-(5-Methoxycarbonyl-3-pyridyloxy)aniline 284462-59-5P, 4-[3-(N-Methylsulfamoyl)phenyloxy]benzene 284462-60-8P, 4-[3-(N-Methylsulfamoyl)phenyloxy]-1-nitrobenzene 284462-61-9P, 4-(3-Methylsulfamoylphenoxy)aniline 284462-62-0P, 4-[4-(1-(Methoxyamino)ethyl)phenoxy]aniline hydrochloride 284462-63-1P, 4-Chloro-N-(2-triisopropylsilyloxy)ethylpyridine-2-carboxamide 284462-64-2P, 4-[[2-[N-(2-Triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]aniline 284462-65-3P, 4-(2-Methoxycarbonyl-5-pyridyloxy)-1-nitrobenzene 284462-66-4P, 4-(2-Methoxycarbonyl-5-pyridyloxy)aniline 284462-74-4P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-methylaniline 284462-77-7P, 5-tert-Butyl-2-methoxyphenyl isocyanate 284462-78-8P, 3-[2-(N-Methylcarbamoyl)-4-pyridyloxy]aniline 284462-79-9P, 3-(2-Carbamoyl-4-pyridyloxy)aniline 284462-80-2P, 4-(2-Carbamoyl-4-pyridyloxy)aniline 284462-82-4P, 4-[2-(N-Ethylcarbamoyl)-4-pyridyloxy]aniline 284462-83-5P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-3-chloroaniline 284462-84-6P 284462-85-7P, 4-(3-Carbamoylphenoxy)aniline 284462-86-8P, 4-[2-(N,N-Dimethylcarbamoyl)-4-pyridyloxy]aniline 284462-89-1P, 4-[2-(N-Isopropylcarbamoyl)-4-pyridyloxy]aniline 284462-92-6P, 3-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-4-methylaniline 284462-93-7P, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]aniline 284462-94-8P, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]aniline 284462-95-9P, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]aniline 284462-99-3P, 4-Chloro-2-methoxy-5-(trifluoromethyl)phenyl isocyanate 284670-99-1P, 4-(4-Acetylphenoxy)-5-aminopyridine 284671-00-7P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 284671-01-8P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[3-carboxyphenyl]urea 573673-51-5P, 4-[4-[2-(N-Methylcarbamoyl)phenyl]thio]aniline 573673-52-6P, 3-[4-[2-(N-Methylcarbamoyl)phenyl]thio]aniline 573673-55-9P, 4-[3-[N-[(1-Methyl-2-pyrrolidinyl)methyl]carbamoyl]phenoxy]aniline 604813-03-8P, 4-(5-Methylcarbamoyl-3-pyridyloxy)aniline 604813-05-0P 604813-07-2P, 4-Chloro-N-ethyl-2-pyridinecarboxamide 604813-08-3P, 4-Chloro-N-isopropyl-2-pyridinecarboxamide 604813-09-4P, 4-[4-(N-Methylsulfamoyl)phenoxy]benzene 604813-11-8P, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-12-9P, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-13-0P, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-14-1P, 4-[3-[N-[(1-Methyl-2-pyrrolidinyl)methyl]carbamoyl]phenoxy]-1-nitrobenzene  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of  $\omega$ -carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

IT	284418-48-2P	284461-33-2P	284461-34-3P	284461-35-4P	284461-36-5P
	284461-37-6P	284461-38-7P	284461-39-8P	284461-40-1P	284461-41-2P
	284461-42-3P	284461-43-4P	284461-44-5P		
	284461-45-6P	284461-46-7P	284461-47-8P		
	284461-48-9P	284461-49-0P	284461-50-3P		
	284461-51-4P	284461-52-5P	284461-53-6P	284461-54-7P	
	284461-55-3P	284461-56-9P	284461-57-0P	284461-58-1P	
	284461-59-2P	284461-60-5P	284461-61-6P	284461-62-7P	
	284461-63-8P	284461-64-9P	284461-65-0P	284461-66-1P	284461-67-2P
	284461-68-3P	284461-70-7P	284461-71-8P	284461-72-9P	
	284461-73-0P	284461-74-1P	284461-75-2P		

284461-76-3P 284461-77-4P 284461-78-5P 284461-79-6P  
 284461-80-9P 284461-81-0P 284461-82-1P  
 284461-83-2P 284461-84-3P 284461-85-4P 284461-88-7P  
 284461-89-8P 284461-90-1P 284461-91-2P 284461-92-3P  
 284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P  
 284461-99-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(3-methylcarbamoylphenyl)carbamoylphenyl]urea 284462-01-7P  
 284462-02-8P 284462-03-9P 284462-04-0P 284462-05-1P  
 284462-07-3P 284462-08-4P 284462-09-5P 284462-10-8P 284462-11-9P  
 284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P  
 284462-17-5P 284462-18-6P 284462-19-7P  
 284462-20-0P 284462-21-1P 284462-22-2P  
 284462-23-3P 284462-24-4P 284462-25-5P 284462-26-6P  
 284462-27-7P 284462-28-8P 284462-29-9P  
 284462-30-2P 284462-31-3P 284462-34-6P  
 284462-35-7P, N-[5-(tert-Butyl)-2-(2,5-dimethylpyrrolyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-36-8P  
 284462-70-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[N-[3-(3-pyridyl)carbamoylphenyl]carbamoylphenyl]urea 284670-98-0P,  
 N,N'-Bis[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 447457-08-1P  
 573673-43-5P 604813-02-7P 604813-04-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[3-[5-(2-dimethylaminoethyl)carbamoyl]pyridyloxy]phenyl]urea 620962-97-2P 620962-98-3P  
 620962-99-4P 620963-00-0P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of  $\alpha$ -carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

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ACCESSION NUMBER: 2003:590832 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:149528

TITLE: Preparation of diphenylureas as RAF kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 62 pp., Cont. of U. S. Ser. No. 42,203.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

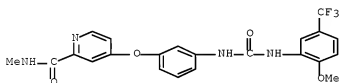
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030144278	A1	20030731	US 2002-283248	20021030 <--
US 7235576	B1	20070626	US 2002-42203	20020111 <--
PRIORITY APPLN. INFO.:			US 2001-367380P	P 20010112 <--
			US 2002-42203	A1 20020111 <--

OTHER SOURCE(S): MARPAT 139:149528

AB ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound directly to D; L1 = substituted cyclic moiety having  $\geq 5$  members, M = bridging group having  $\geq 1$  atom; q = 1-3; L, L1 contain 0-4 N, O, S; B = (substituted) up to tricyclic aryl, heteroaryl of  $\leq 30$  C atoms with  $\geq 1$  6-membered cyclic

structure bound directly to D containing O-4 N, O, S], were prepared Thus, 4-chloro-3-(trifluoromethyl)phenyl isocyanate in CH<sub>2</sub>Cl<sub>2</sub> was added dropwise to a suspension of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (preparation given) in CH<sub>2</sub>Cl<sub>2</sub> at 0°; the resulting mixture was stirred at room temperature for 22 h. to afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1 µM. I pharmaceutical comps. are claimed.

- IT 284461-42-3P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of diphenylureas as RAF kinase inhibitors)  
 RN 284461-42-3 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



- IC ICM A61K031-541  
 ICS A61K031-5377; A61K031-496; A61K031-454; A61K031-4025; C07D417-02; C07D413-02; C07D043-02  
 INCL 514227800; 514231500; 514252130; 514326000; 514422000; 544060000; 544111000; 544359000; 546207000  
 CC 27-16 (Heterocyclic Compounds (One Hetero Atom))  
 Section cross-reference(s): 1, 25, 63  
 IT 228418-48-2P 284461-33-2P, N-(3-tert-Butylphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl] urea 284461-34-3P, N-(3-tert-Butylphenyl)-N'-[4-(4-acetylphenoxy)phenyl] urea 284461-35-4P 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-37-6P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-38-7P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisindolin-5-yloxy)phenyl]urea 284461-39-8P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisindolin-5-yloxy)phenyl] urea 284461-40-1P 284461-41-2P 284461-42-3P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284461-43-4P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl] urea 284461-44-5P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284461-45-6P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl] urea 284461-46-7P 284461-47-8P 284461-48-9P 284461-49-0P 284461-50-3P 284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(1,3-dioxoisindolin-5-yloxy)phenyl] Urea 284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridylthio]phenyl] urea 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P 284461-63-8P 284461-64-9P

284461-65-0P 284461-66-1P 284461-67-2P 284461-68-3P 284461-69-4P  
 284461-70-7P 284461-71-8P 284461-72-9P 284461-73-0P,  
 N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-76-3P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-77-4P 284461-78-5P 284461-80-9P 284461-81-0P 284461-82-1P 284461-83-2P 284461-84-3P 284461-85-4P 284461-88-7P 284461-89-8P 284461-90-1P 284461-91-2P 284461-92-3P 284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P 284461-98-9P 284461-99-0P 284462-00-6P 284462-01-7P 284462-02-8P 284462-03-9P 284462-04-0P 284462-05-1P 284462-07-3P 284462-08-4P 284462-09-5P 284462-10-8P 284462-11-9P 284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P 284462-17-5P 284462-18-6P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-19-7P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[2-chloro-4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-20-9P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-chloro-4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-21-1P 284462-22-2P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-23-3P 284462-24-4P 284462-25-5P 284462-26-6P 284462-27-7P 284462-28-8P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284462-29-9P 284462-30-2P 284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284462-32-4P 284462-34-6P 284462-35-7P 284462-67-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-aminophenyl) Urea 284462-68-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-ethoxycarbonylphenyl)urea 284462-70-0P 284462-97-1P 284670-98-0P 447457-08-1P 447457-09-2P 474642-51-8P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-carboxyphenyl)urea 474642-55-2P 573673-42-4P 573673-43-5P 573673-45-7P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of diphenylureas as RAF kinase inhibitors)  
 IT 98-98-6, Picolinic acid 100-51-6, Benzyl alcohol, reactions 106-50-3, p-Phenylenediamine, reactions 108-00-9 109-85-3 110-13-4, Acetonylacetone 110-91-8, Morpholine, reactions 123-30-8, 4-Aminophenol 123-39-7 320-51-4, 4-Chloro-3-trifluoromethylaniline 327-78-6, 4-Chloro-3-trifluoromethylphenyl isocyanate 349-65-5 350-46-9 393-36-2 462-08-8, 3-Pyridinamine 593-56-6, O-Methylhydroxylamine hydrochloride 610-35-5, 4-Hydroxyphthalic acid 619-08-9 626-61-9 883-99-8, Methyl 3-hydroxy-2-naphthoate 1121-78-4 1215-98-1 1664-40-0 1877-71-0 2038-03-1, 4-Morpholineethanamine 2835-99-6, 4-Amino-3-methylphenol 2905-24-0 3535-88-4 5369-19-7 6310-19-6, 2-Nitro-4-tert-butylaniline 6628-77-9 6927-86-2 7781-98-8 16588-75-3 25900-61-2 29264-35-5 30766-22-4 30806-83-8 34803-66-2 36265-31-3 51639-48-6 73441-86-8 150009-83-9 256340-75-7 284461-86-5 284462-06-2 284462-44-8 284462-71-1 284462-72-2 284462-73-3 284462-74-4 284462-76-6 284462-77-7 284462-78-8 284462-79-9 284462-80-2 284462-82-4 284462-84-6 284462-85-7 284462-86-8 284462-89-1 284462-92-6 284462-93-7 284462-94-8 284462-95-9 284462-99-3 284670-99-1



284671-01-8 573673-48-0 573673-49-1 573673-50-4 573673-51-5  
 573673-52-6 573673-53-7 573673-55-9 573673-56-0  
 573673-58-2 573673-59-3 573673-60-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of diphenylureas as RAF kinase inhibitors)

L110 ANSWER 47 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:123969 HCAPLUS Full-text

DOCUMENT NUMBER: 141:166948

TITLE: Raf pathway inhibitors in oncology

AUTHOR(S): Bollag, Gideon; Freeman, Scott; Lyons, John F.; Post, Leonard E.

CORPORATE SOURCE: Plexxikon Inc, Berkeley, CA, 94710, USA

SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(12), 1436-1441  
 CODEN: COIDA3; ISSN: 1472-4472

PUBLISHER: Thomson Current Drugs

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Recognition of the importance of the Raf pathway in the proliferation and survival of tumor cells recently increased with the discovery of activating BRAF mutations in human tumors. Therefore, in addition to a role in controlling tumors with Ras mutations and activated growth factor receptors, inhibitors of the Raf pathway may harbor therapeutic potential in tumors carrying a BRAF oncogene. A variety of agents have been discovered that interfere with the Raf pathway, including antisense oligonucleotides and small mols. These inhibitors block the expression of Raf protein, block Ras/Raf interaction, block its kinase activity, or block the kinase activity of the Raf target protein mitogen-activated protein kinase kinase. Raf pathway inhibitors that are currently undergoing clin. evaluation show promising signs of anticancer efficacy with a very tolerable safety profile. Indeed, the Raf inhibitor BAY-43-9006 recently entered phase III clin. trials. Here, we review the current development status of potential Raf pathway therapeutics.

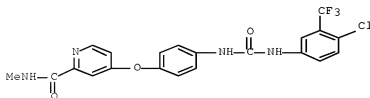
IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Raf pathway inhibitors were currently in clin. trial and showed promising anticancer efficacy with very tolerable safety profile and BAY-43-9006 recently entered phase III clin. trial)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 284461-73-0, BAY-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(Raf pathway inhibitors were currently in clin. trial and showed promising anticancer efficacy with very tolerable safety profile and BAY-43-9006 recently entered phase III clin. trial)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 48 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:736198 HCAPLUS Full-text

DOCUMENT NUMBER: 139:301125

TITLE: BAY-43-9006 (Bayer/Onyx)

AUTHOR(S): Lee, John T.; McCubrey, James A.

CORPORATE SOURCE: Department of Microbiology and Immunology, Brody School of Medicine at East Carolina University, Greenville, NC, 27858-4353, USA

SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(6), 757-763  
CODEN: COIDAZ; ISSN: 1472-4472

PUBLISHER: Thomson Current Drugs

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

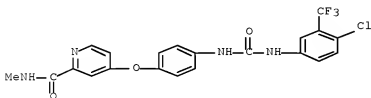
AB A review. Bayer and Onyx are developing BAY-43-9006, an oral cytostatic Raf kinase inhibitor for the potential treatment of colorectal and breast cancers, hepatocellular carcinoma and non-small-cell lung cancer, in addition to acute myelogenous leukemia, myelodysplastic syndrome and other cancers. A US IND was filed in May 2000 and by Feb. 2003 BAY-43-9006 was in phase II trials, with phase III trials expected to begin later in 2003.

IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BAY 43-9006 for treatment of cancer patients)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 284461-73-0, BAY 43-9006

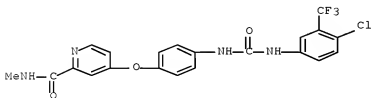
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BAY 43-9006 for treatment of cancer patients)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 49 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12708 HCAPLUS Full-text

DOCUMENT NUMBER: 140:70551  
 TITLE: A Phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors  
 AUTHOR(S): Richly, H.; Kupsch, P.; Passage, K.; Grubert, M.; Hilger, R. A.; Kredtke, S.; Voliotis, D.; Scheulen, M. E.; Seeber, S.; Strumberg, D.  
 CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany  
 SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 620-621  
 CODEN: ICTHEK; ISSN: 0946-1965  
 PUBLISHER: Dustri-Verlag Dr. Karl Feistle  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Objective: The primary objective of this phase I study was to define the safety profile of BAY 43-9006 administered in combination with doxorubicin. Patients and methods: Twenty-nine patients with advanced, refractory solid tumors were treated with doxorubicin (60mg/m<sup>2</sup>) every 3 wk for 6 consecutive cycles. BAY 43-9006 in combination with doxorubicin chemotherapy was administered at 3 dose levels. Results: Toxicity and response were evaluable in a total of 24 out of 29 enrolled patients. Dose-limiting toxicity was observed at various dose levels. Doxorubicin plasma Cmax/AUC values increased on escalating the dose of BAY 43-9006. Patients with liver metastases and elevated values of AST and conjugated bilirubin, compared to patients with normal hepatic function, showed a higher AUC for doxorubicin at all dose levels. Conclusions: Our data suggest a pharmacol. interaction of BAY 43-9006 at DL 400 mg bid with doxorubicin resulting in significantly increased AUC for doxorubicin.  
 IT 284461-73-0, BAY 43-9006  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)  
 RN 284461-73-0 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-6 (Pharmacology)  
 IT 284461-73-0, BAY 43-9006  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 50 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12707 HCAPLUS Full-text

DOCUMENT NUMBER: 140:70550

TITLE: Drug-drug interaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors

AUTHOR(S): Mross, K.; Steinbild, S.; Baas, F.; Reil, M.; Buss, P.; Mersmann, S.; Voliotis, D.; Schwartz, B.; Brendel, E.

CORPORATE SOURCE: Tumor Biology Center at the Albert-Ludwigs-University Freiburg, Leverkusen, Germany

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 618-619

CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Classical cytotoxic anticancer drugs generally have specific actions but also interfere with signalling pathways. A logical approach is therefore to combine the Raf kinase inhibitor (RKI) with classical cytotoxic agents since recent work has shown that the RKI BAY 43-9006 and CPT-11 have additive or synergistic actions. Objective: Because a pharmacol. drug-drug interaction cannot be ruled out, interaction studies were started using the RKI BAY 43-9006 in combination with the most important anticancer drugs, such as CPT-11. Patients and methods: The study protocol included three groups of 6 patients with solid tumors given different RKI doses and the same dosage of CPT-11. Blood samples for measurement of CPT-11 and SN-38 were obtained both during and in the absence of RKI treatment. Results: Ests. of toxicity, response and pharmacokinetics during the first RKI dose could be made in a total of 9/18 patients. All symptoms of toxicity were considered to be due to CPT-11 or RKI. The PK evaluation showed no significant differences for CPT-11 and SN-38, with or without RKI. Conclusions: The combination CPT-11 and SN-38 PK is not significantly influenced by the addition of RKI. There is no indication that the PK of RKI are influenced significantly by CPT-11 and SN-38.

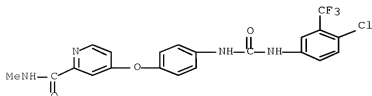
IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-6 (Pharmacology)  
 IT 284461-73-0, BAY 43-9006  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)  
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 51 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:12706 HCAPLUS Full-text

DOCUMENT NUMBER: 141:17009

TITLE: Antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006  
 AUTHOR(S): Heim, M.; Sharifi, M.; Hilger, R. A.; Scheulen, M. E.; Seeber, S.; Strumberg, D.

CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany

SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 616-617  
 CODEN: ICTHEK; ISSN: 0946-1965

PUBLISHER: Dustri-Verlag Dr. Karl Feistle

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A study was conducted to evaluate the effects of combining BAY 43-9006 and cytotoxic drugs (paclitaxel, 5-FU, oxaliplatin, and SN-38) on human cancer cells using 4 sequencing protocols and to analyze the effect of RKI on colorectal cancer cells showing marked resistance against SN-38. Results showed the additive action or moderate synergy using RKI in combination with numerous cytotoxic agents and the marked reduction of oxaliplatin activity by RKI in human carcinoma cells. These indicate that Raf kinase activity might be important for oxaliplatin-induced cytotoxicity. Furthermore, lacking cross-resistance between SN-38 and RKI might provide a rationale for designing clinical trials using CPT-11 in combination with BAY 43-9006 in patients with colorectal cancer.

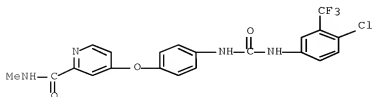
IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006 in relation to resistance to SN-38)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)

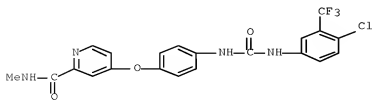


CC 1-6 (Pharmacology)  
 IT 51-21-8, 5-FU 33069-62-4, Paclitaxel 61825-94-3, Oxaliplatin  
 86639-52-3, SN-38 284461-73-0, BAY 43-9006  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (antitumor effect and potentiation or reduction in cytotoxic drug activity  
 in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY  
 43-9006 in relation to resistance to SN-38)  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 52 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:12705 HCAPLUS Full-text  
 DOCUMENT NUMBER: 140:349958  
 TITLE: Circadian rhythm in the regulation of the MAP kinase  
 pathway - pitfall in the determination of surrogate  
 parameters?  
 AUTHOR(S): Hilger, R. A.; Diaz-Carballo, D.; Bauer, S.; Kredtke,  
 S.; Scheulen, M. E.; Seeber, S.; Strumberg, D.  
 CORPORATE SOURCE: Department of Internal Medicine (Cancer Research),  
 West German Cancer Center, University of Essen Medical  
 School, Essen, Germany  
 SOURCE: International Journal of Clinical Pharmacology and  
 Therapeutics (2003), 41(12), 614-615  
 CODEN: ICTHEK; ISSN: 0946-1965  
 PUBLISHER: Dustri-Verlag Dr. Karl Feistle  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A method for the quantification of the inhibitory potency of BAY 43-9006, a  
 novel potent and orally active inhibitor of Raf kinase, measuring the  
 phosphorylated (activated) extracellular signal-regulated kinase (ERK) as a  
 biomarker, was developed. A circadian rhythm in phosphorylation of ERK1/2  
 proteins after phorbol myristate acetate stimulation was observed. It was  
 demonstrated that biomarker measurements could be complicated by circadian  
 variability of the specific mol. target. Phosphorylated ERK1/2 may serve as a  
 biomarker for drugs targeting the mitogen-activated protein kinase cascade.  
 However, the demonstrated circadian regulation demands strict protocols for  
 the realization of biomarker analyses.

IT 284461-73-0, BAY 43-9006  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (circadian rhythm in regulation of MAP kinase pathway)  
 RN 284461-73-0 HCAPLUS  
 CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-1 (Pharmacology)  
 IT 284461-73-0, BAY 43-9006  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (circadian rhythm in regulation of MAP kinase pathway)  
 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 53 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:476541 HCAPLUS Full-text

DOCUMENT NUMBER: 139:143192

TITLE: Activity of the Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors

AUTHOR(S): DeGrendele, Heather

CORPORATE SOURCE: USA

SOURCE: Clinical Colorectal Cancer (2003), 3(1), 16-18

CODEN: CCCLCF; ISSN: 1533-0028

PUBLISHER: Cancer Information Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. BAY 43-9006 is the first orally active Raf kinase inhibitor to undergo clin. testing and has shown promise in the treatment of colorectal cancer. Treatment with BAY 43-9006 has resulted in stable disease in 37 % of patients across this phase I series, with 42 % of colorectal cancer patients achieving stable disease. Among patients achieving stable disease, 27 have been on therapy for over 6 mo without progression. Toxicity associated with this regimen is mild, with few grade 3/4 adverse events reported. Furthermore, fluorescence-activated cell sorter (FACS) anal. demonstrated that treatment with BAY 43-9006 could result in the inhibition of extracellular signal-regulated kinase (ERK) activation. Based on this phase I data, 2 phase II trials, including one in patients with colorectal cancer, have been initiated, and phase III trials are planned for 2003. At the 38th Annual Meeting of the American Society of Clin. Oncol., Vincent and colleagues reported on preclin. studies combining BAY 43-9006 with irinotecan, vinorelbine, or gemcitabine in human xenografts models. They demonstrated that BAY 43-9006 combined with cytotoxic or cytostatic agents is at least as efficacious as the individual agents administered alone. With this as rationale, multiple phase I/II studies are being designed to investigate the role of BAY 43-9006 in combination with standard chemotherapy.

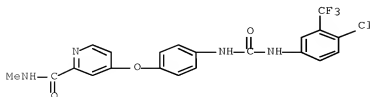
IT 284461-73-0, BAY 43-9006

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)

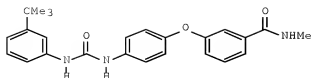


CC 1-0 (Pharmacology)  
 IT 284461-73-0, BAY 43-9006  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)  
 REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 54 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2002:615574 HCAPLUS Full-text  
 DOCUMENT NUMBER: 137:169425  
 TITLE: Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors  
 INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.  
 PATENT ASSIGNEE(S): Bayer Corporation, USA  
 SOURCE: PCI Int. Appl., 125 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062763	A2	20020815	WO 2002-US3361	20020207 <--
WO 2002062763	A3	20021010		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20020165394	A1	20021107	US 2001-777920	20010207 <--
AU 2002238042	A1	20020819	AU 2002-238042	20020207 <--
AU 2004200722	A1	20040318	AU 2004-200722	20040224 <--
AU 2004200722	B2	20080110		
PRIORITY APPLN. INFO.:			US 2001-777920	A 20010207 <--
			US 1999-115877P	P 19990113 <--
			US 1999-257266	B2 19990225 <--
			US 1999-425228	B2 19991022 <--
			AU 2000-25016	A3 20000112 <--
			US 2001-758548	A2 20010112 <--
			WO 2002-US3361	W 20020207 <--
OTHER SOURCE(S):	MARPAT 137:169425			
GI				





II

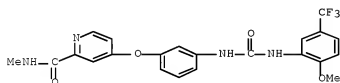
AB Title compds., e.g., RNHCONHZOR1 [I; R = C<sub>6</sub>H<sub>4</sub>(CMe<sub>3</sub>)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepared. Thus, 4-(H<sub>2</sub>N)C<sub>6</sub>H<sub>4</sub>OC<sub>6</sub>H<sub>4</sub>(CONHMe)-4 (preparation given) was condensed with 3-(Me<sub>3</sub>C)C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub> and CO(OCCl<sub>3</sub>)<sub>2</sub> to give title compound II. Data for biol. activity of title compds. were given.

IT 284461-42-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D215-38

ICS C07D401-12; A61K031-4406; A61K031-47; A61P035-00; C07D401-12;  
C07D215-00; C07D213-00; C07D401-12; C07D215-00; C07D209-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P  
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 447457-09-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase  
 inhibitors)

L110 ANSWER 55 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:314913 HCAPLUS Full-text

DOCUMENT NUMBER: 136:340689

TITLE: Preparation of urea derivatives containing nitrogenous  
 aromatic ring compounds as inhibitors of angiogenesis  
 INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura,  
 Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata,  
 Junichi; Takahashi, Keiko; Matsushima, Tomohiro;  
 Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo;  
 Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi;  
 Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji;  
 Matsui, Junji; Matsui, Kenji; Yoshida, Takako; Suzuki,  
 Yasuyuki; Arimoto, Itaru

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 699 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese

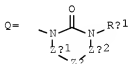
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032872	A1	20020425	WO 2001-JP9221	20011019 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2426461	A1	20020425	CA 2001-2426461	20011019 <--
AU 2001095986	A	20020429	AU 2001-95986	20011019 <--
HU 2003002603	A2	20031128	HU 2003-2603	20011019 <--
CN 1478078	A	20040225	CN 2001-819710	20011019 <--
EP 1415987	A1	20040506	EP 2001-976786	20011019 <--
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

## 10/590724

EP 1506962	A2	20050216	EP 2004-25700	20011019 <--
EP 1506962	A3	20050302		
EP 1506962	B1	20080702		
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NZ 525324	A	20050324	NZ 2001-525324	20011019 <--
JP 3712393	B2	20051102	JP 2002-536056	20011019 <--
RU 2264389	C2	20051120	RU 2003-114740	20011019 <--
AT 355275	T	20060315	AT 2001-976786	20011019 <--
AU 2001295986	B2	20060817	AU 2001-295986	20011019 <--
EP 1777218	A1	20070425	EP 2006-23078	20011019 <--
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CN 101024627	A	20070829	CN 2007-10007096	20011019 <--
CN 101029022	A	20070905	CN 2007-10007097	20011019 <--
ES 2282299	T3	20071016	ES 2001-976786	20011019 <--
NO 2003001731	A	20030619	NO 2003-1731	20030414 <--
MX 2003PA03362	A	20030801	MX 2003-PA3362	20030415 <--
US 7253286	B2	20070807	US 2003-420466	20030418 <--
US 20040053908	A1	20040318		
ZA 2003003567	A	20040810	ZA 2003-3567	20030508 <--
JP 2005272474	A	20051006	JP 2005-124034	20050421 <--
US 20060247259	A1	20061102	US 2005-293785	20051202 <--
US 20060160832	A1	20060720	US 2006-347749	20060203 <--
AU 2006203099	A1	20060810	AU 2006-203099	20060719 <--
AU 2006236039	A1	20061207	AU 2006-236039	20061116 <--
AU 2006236039	B2	20080522		
NO 2007004657	A	20030619	NO 2007-4657	20070912 <--
PRIORITY APPLN. INFO.:				
			JP 2000-320420	A 20001020 <--
			JP 2000-386195	A 20001220 <--
			JP 2001-46685	A 20010222 <--
			AU 2001-295986	A3 20011019 <--
			AU 2001-95986	TO 20011019 <--
			CN 2001-819710	A3 20011019 <--
			EP 2001-976786	A3 20011019 <--
			JP 2002-536056	A3 20011019 <--
			WO 2001-JP9221	W 20011019 <--
			US 2003-420466	A3 20030418 <--
			US 2005-293785	A1 20051202
OTHER SOURCE(S): MARPAT 136:340689				
GI				



AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14

aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH<sub>2</sub>)<sub>g</sub>SO<sub>2</sub> (g = 1-8), (CH<sub>2</sub>)<sub>fa</sub>CH:CH(CH<sub>2</sub>)<sub>fb</sub> (fa, fb = 0, 1, 2, 3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl are prepared. These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC<sub>50</sub> of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT 417714-74-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

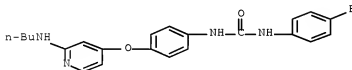
(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-74-0 HCAPLUS

CN Urea, N-[4-[[2-(butylamino)-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)-  
(CA INDEX NAME)



IC ICM C07D213-74

ICS C07D213-75; C07D215-48; C07D239-47; C07D401-12; C07D401-14;  
C07D413-12; C07D405-12; C07D409-12; C07D413-12; C07D417-12;  
C07D417-14; C07D471-14; C07D491-048; C07D495-04; A61K031-4709;  
A61K031-47; A61K031-5377; A61K031-496; A61K031-4545

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): i, 27

IT	398487-65-5P	417712-82-4P	417712-83-5P	417712-84-6P	417712-85-7P
	417712-86-8P	417712-87-9P	417712-88-0P	417712-89-1P	417712-90-4P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.)

as

angiogenesis inhibitors for prevention or treatment of diseases)

IT

417715-71-0P	417715-72-1P	417715-73-2P	417715-74-3P	417715-75-4P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

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	17576-39-5P	17614-10-7P	18031-97-5P	39142-40-0P, Phenyl	
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

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 ((3-bromopropionyl)amino)-4-pyridyl]oxy]-1H-1-indolecarboxamide  
 417724-88-0P, 4-[2-[(4-[3-Chloro-4-(phenoxycarbonyl)amino]phenoxy)-2-  
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 hydroxyquinoline 417725-09-8P, 2-Amino-4-(4-nitrophenoxy)-3-  
 nitropyridine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

angiogenesis inhibitors for prevention or treatment of diseases)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 56 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:850357 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 137:352907

TITLE: Preparation of quinolyl, isoquinolyl or pyridyl-ureas  
 as inhibitors of raf kinase for the treatment of  
 tumors and/or cancerous cell growth

INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill  
 E.; Robert, Sibley N.; Monahan, Mary-Katherine;  
 Renick, Joel; Gunn, David E.; Lowinger, Timothy B.;  
 Scott, William J.; Smith, Roger A.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S.  
 Ser. No. 758,548.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020165394	A1	20021107	US 2001-777920	20010207 <--



CA 2549558	A1	20000720	CA 2000-2549558	20000112 <--
CN 1721397	A	20060118	CN 2005-10089504	20000112 <--
EP 1690853	A1	20060816	EP 2005-28442	20000112 <--
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ZA 2001005751	A	20030714	ZA 2001-5751	20010712 <--
US 20020137774	A1	20020926	US 2001-907970	20010719 <--
WO 2002062763	A2	20020815	WO 2002-US3361	20020207 <--
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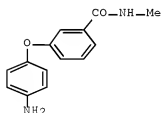
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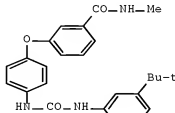
## OTHER SOURCE(S):

MARPAT 137:352907

GI



II



III

AB Title compds. B-NHCONH-L-(M-L1)q (I) [B = (un)substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and

S] and their pharmaceutically acceptable salts were prepared. For example, coupling of aniline II, e.g., prepared from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butylaniline afforded urea III. In vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC50 values ranging from 10 nM-10 µM. Compds. I are useful for the treatment of cancerous cell growth mediated by raf kinase.

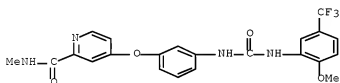
IT 284461-41-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D217-22

ICS C07D215-38

INCL 546143000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

L110 ANSWER 57 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:732413 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:362126

TITLE: Benzodiazepine inhibitors of the MMPs and TACE

AUTHOR(S): Nelson, Frances C.; Delos Santos, Efren; Levin, Jeremy I.; Chen, James M.; Skotnicki, Jerald S.; DiJoseph, John F.; Sharr, Michele A.; Sung, Amy; Killar, Loran M.; Cowling, Rebecca; Jin, Guixian; Roth, Catherine E.; Albright, J. Donald

CORPORATE SOURCE: Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002

), 12(20), 2867-2870

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:362126

AB A series of benzodiazepine inhibitors of the MMPs and TACE has been developed. These compds. display an interesting selectivity profile and should be useful tools for exploring the biol. relevance of such selectivity.

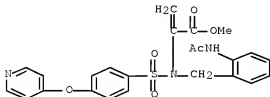
IT 522623-58-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(benzodiazepine inhibitors of MMPs and TACE)

RN 522623-58-1 HCAPLUS

CN 2-Propenoic acid, 2-[[[2-(acetylamino)phenyl]methyl][[4-(4-pyridinyloxy)phenyl]sulfonyl]amino]-, methyl ester (CA INDEX NAME)



CC 1-3 (Pharmacology)

IT 85622-74-8P 232950-28-6P 233754-49-9P 233754-50-2P 233754-53-5P  
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 522623-87-6P 597564-87-9P 612491-93-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(benzodiazepine inhibitors of MMPs and TACE)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 58 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:785445 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 138:296904

TITLE: BAY 43-9006: Preclinical data

AUTHOR(S): Wilhelm, Scott; Chien, Du-Shieng

CORPORATE SOURCE: Bayer Research Center, Institute for Preclinical Drug  
 Development, Pharmaceutical Division, Bayer  
 Corporation, West Haven, CT, 06516, USA  
 SOURCE: Current Pharmaceutical Design (2002), 8(25),  
 2255-2257

CODEN: CPDEFF; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

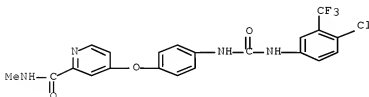
AB A review. The drug design and discovery efforts described in the previous  
 section led to the development of a novel, small mol. Raf-1 kinase inhibitor,  
 BAY 43-9006, which belongs to a class that can be broadly described as bis-  
 aryl ureas. BAY 43-9006 was identified during a large medicinal chemical  
 optimization program, and this compound was selected for further pharmacol.  
 characterization based on its potent inhibition of Raf-1 (IC50 12 nM) and its  
 favorable kinase selectivity profile [2, 3]. In vitro and in vivo expts. were  
 designed to demonstrate effective blockade of the Raf/MEK/ERK signaling  
 pathway in tumor cells and for antitumor efficacy in human xenograft models.

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antitumor BAY 43-9006)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c  
 arboxyl]aminophenyl]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 284461-73-0, BAY 43-9006

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antitumor BAY 43-9006)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

L110 ANSWER 59 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:785444 HCAPLUS Full-text

DOCUMENT NUMBER: 137:362317

TITLE: BAY 43-9006: Early clinical data in patients with advanced solid malignancies

AUTHOR(S): Hotte, Sebastien J.; Hirte, Hal W.

CORPORATE SOURCE: Department of Medicine, Hamilton Regional Cancer Centre, McMaster University and Division of Medical Oncology, Hamilton, ON, Can.

SOURCE: Current Pharmaceutical Design (2002), 8(25), 2249-2253

CODEN: CPDEFF; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Various signaling pathways can confer the malignant phenotype to a cell. Ras signaling proteins have been found to play an important role in controlling cellular growth. Raf-1 is a protein kinase that exerts its effects downstream of Ras in the mitogen-activated protein kinase pathway and is thus likely to be crucial in the development of the malignant phenotype. BAY 43-9006 is an orally administered selective inhibitor of Raf-1 and the first compound of its class to enter clin. trials. This article describes the early clin. data of BAY 43-9006 in patients with advanced, refractory solid tumors. To date, over 60 patients have been treated as part of four Phase I clin. trials. Dose levels have ranged from 50mg once weekly to 200mg twice-daily in continuous administration. The drug has been generally well tolerated with no dose limiting toxicity yet encountered. The more common toxicities have involved the gastrointestinal tract (diarrhea, nausea, abdominal cramping) and the skin (pruritus, rash, cheilitis). Pharmacokinetic evaluations have found BAY 43-9006 to have considerable interpatient variability. However, there seems to be an increase in Cmax and AUC values with increasing dose. There is no clear effect of food on bioavailability. Splitting the dose to twice-daily administration has shown increases in Cmax and AUC values but is also accompanied by considerable interpatient variability.

IT 475207-59-1, BAY 43-9006 mono-p-tosylate  
 RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (BAY 43-9006 for patients with advanced solid neoplasm)

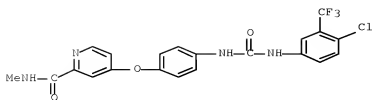
RN 475207-59-1 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 284461-73-0

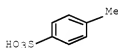
CMF C21 H16 C1 F3 N4 O3



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



CC 1-0 (Pharmacology)

IT 475207-59-1, BAY 43-9006 mono-p-tosylate

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (BAY 43-9006 for patients with advanced solid neoplasm)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 60 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:208292 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 139:269975

TITLE: Oncolytic Raf kinase inhibitor

AUTHOR(S): Sorbera, L. A.; Castaner, J.; Bozzo, J.; Leeson, P. A.

CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain

SOURCE: Drugs of the Future (2002), 27(12),

1141-1147

CODEN: DRFUD4; ISSN: 0377-8282

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with refs. The Ras/Raf/MEK pathway is a signaling module that controls cell growth and survival. Activation of this pathway results in a cascade of events from the cell surface to the nucleus ultimately affecting cellular proliferation, apoptosis, differentiation and transformation. Raf is a serine/threonine kinase that is a downstream effector enzyme of Ras. When activated, Raf goes on to activate MEK1 and MEK2 kinases which in turn phosphorylate and activate ERK1 and ERK2 which translocate to the nucleus where they stimulate pathways required for translation initiation and transcription activation leading to proliferation. Raf kinase has been validated as a potential and attractive target for hyperproliferative disorders such as cancer. Research has recently focused on efforts to discover potent Raf kinase inhibitors and several low-mol.-weight Raf kinase inhibitors have been described. Bis-aryl ureas were identified within this program using

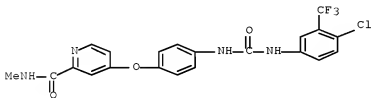
medicinal chemical-directed syntheses or combinatorial libraries. After high-throughput screening of more than 200,000 compds. against recombinant Raf-1 kinase, the orally active Bay-43-9006 was identified as having potent inhibitory activity and was chosen for further development as a treatment for cancer. Bay-43-9006 has exhibited potent in vitro activity against several tumor cell lines and has displayed efficacy in human tumor xenograft models. Moreover, results from phase I development in patients with a variety of cancer types indicates promising clin. efficacy for the compound

IT 284461-73-0, Bay-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(oncolytic Raf kinase inhibitor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 139691-76-2, Raf kinase 284461-73-0, Bay-43-9006

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(oncolytic Raf kinase inhibitor)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 61 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:493516 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 133:120157

TITLE: Preparation of *o*-carboxy(hetero)aryl substituted diphenyl ureas as raf kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA  
SOURCE: PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042012	A1	20000720	WO 2000-US648	20000112 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW  
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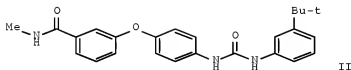
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 KR 2007020158 A 20070216 KR 2007-702656 20070201 <--  
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 IN 2007MN01633 A 20071214 IN 2007-MN1633 20071005 <--  
 US 20080153823 A1 20080626 US 2007-956111 20071213 <--  
 US 1999-115877P P 19990113 <--

PRIORITY APPLN. INFO.:



US 1999-257266	A2 19990225 <--
US 1999-425228	A2 19991022 <--
US 1999-115878P	P 19990113 <--
AU 2000-25016	A3 20000112 <--
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JP 2000-593580	A3 20000112 <--
WO 2000-US648	W 20000112 <--
IN 2001-MN799	A3 20010705 <--
KR 2001-708847	A3 20010712 <--
US 2001-948915	A1 20010910 <--
US 2002-889227	A1 20020108 <--

OTHER SOURCE(S): MARPAT 133:120157  
GI



AB This invention relates to the preparation and use of (hetero)aryl ureas ANHCONHB (I; A = L(ML)q; L = 5- or 6-membered (hetero)aryl, especially Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepared For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addition of 4-(3-N-methylcarbamoylphenoxy)aniline (preparation given) to afford the urea II.

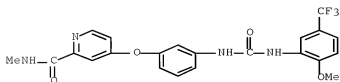
IT 284461-42-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of  $\omega$ -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D211-78  
 ICS C07D211-72; A61K031-33; A61K031-54; A61K031-535; A61K031-17;  
 C07C275-20; C07C275-22; C07C275-24; C07C275-28

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1

IT 284461-13-2P, N-(3-tert-Butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl)urea 284461-34-3P, N-(3-tert-Butylphenyl)-N'-(4-(4-(4-acetylphenoxy)phenyl)urea 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-(4-[3-(N-methylcarbamoyl)phenoxy]phenyl)urea 284461-37-6P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-(4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl)urea 284461-39-8P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-(4-(1-oxoisindolin-5-yl)oxy)phenyl)urea 284461-42-3P 284461-43-4P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl)urea 284461-44-5P 284461-45-6P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl)urea 284461-51-4P 284461-54-7P 284461-58-1P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-(4-[[2-(N-methylcarbamoyl)-4-pyridyl]thio]phenyl)urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl)urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl)urea 284461-78-5P 284461-86-5P 284461-90-1P 284461-99-0P 284462-05-1P 284462-06-2P 284462-17-5P 284462-18-6P 284462-19-7P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-(2-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl)urea 284462-20-0P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-(3-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl)urea 284462-22-2P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-(3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl)urea 284462-26-6P 284462-28-2P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-(4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl)urea 284462-30-2P 284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-(3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl)urea 284462-35-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of  $\omega$ -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

IT 228418-48-2P 284461-35-4P 284461-40-1P 284461-41-2P 284461-46-7P 284461-47-8P 284461-49-0P 284461-50-3P 284461-52-5P 284461-53-6P 284461-55-8P 284461-56-9P 284461-57-0P 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P 284461-63-8P 284461-64-9P 284461-65-0P 284461-66-1P 284461-67-2P 284461-68-3P 284461-69-4P 284461-70-7P 284461-71-8P 284461-72-9P 284461-77-4P 284461-79-6P 284461-80-9P 284461-81-0P 284461-82-1P 284461-83-2P 284461-84-3P 284461-85-4P 284461-88-7P 284461-91-2P 284461-92-3P 284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P 284461-98-9P 284462-00-6P 284462-01-7P 284462-02-8P 284462-03-9P 284462-04-0P 284462-07-3P 284462-08-4P 284462-09-5P 284462-10-8P 284462-11-9P 284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P 284462-21-1P 284462-23-3P 284462-24-4P 284462-25-5P 284462-27-7P 284462-32-4P 284462-33-5P 284462-34-6P 284462-36-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of  $\omega$ -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

- IT 98-98-6, Picolinic acid 99-98-9, 4-(Dimethylamino)aniline 106-50-3, p-Phenylenediamine, reactions 108-00-9, N,N-Dimethylethylenediamine 109-85-3, 2-Methoxyethylamine 110-13-4, Acetylacetone 123-30-8, 4-Aminophenol 320-51-4, 4-Chloro-3-(trifluoromethyl)aniline 327-78-6, 4-Chloro-3-(trifluoromethyl)phenyl isocyanate 349-65-5, 2-Methoxy-5-(trifluoromethyl)aniline 350-46-9, 1-Fluoro-4-nitrobenzene 371-40-4, 4-Fluoroaniline 393-36-2, 4-Bromo-3-(trifluoromethyl)aniline 462-08-8, 3-Aminopyridine 610-35-5, 4-Hydroxyphthalic acid 619-08-9, 2-Chloro-4-nitrophenol 626-61-9, 4-Chloropyridine 883-99-8, Methyl 3-hydroxy-2-naphthoate 1121-78-4, 5-Hydroxy-2-methylpyridine 1215-98-1, 4-(4-Acetylphenoxy)aniline 1664-40-0, N-Phenylethylenediamine 1877-71-0, Monomethyl isophthalate 2038-03-1, 4-(2-Aminoethyl)morpholine 2252-63-3, N-(4-Fluorophenyl)piperazine 2524-67-6, 4-Morpholinolaniline 2835-99-6, 4-Amino-3-methylphenol 2905-24-0, 3-Bromobenzenesulfonyl chloride 5369-19-7, 3-tert-Butylaniline 6310-19-6, 2-Nitro-4-tert-butylaniline 6628-77-9, 5-Amino-2-methoxypyridine 6927-86-2, 4-(4-Acetylphenoxy)aniline hydrochloride 7781-98-8, Ethyl 3-hydroxybenzoate 13154-24-0, Triisopropylsilyl chloride 16588-75-3 25900-61-2, 3-(Methylcarbamoyl)aniline 29264-35-5, 4-(3-Carboxy-4-hydroxyphenoxy)-1-nitrobenzene 30766-22-4, Methyl 5-hydroxynicotinate 30806-83-8, Ethyl 4-isocyanatobenzoate 34803-66-2, N-(2-Pyridyl)piperazine 36265-31-3, 4-(4-Methylthiophenoxy)-1-nitrobenzene 51639-48-6, N-(4-Acetylphenyl)piperazine 73441-86-8 150009-83-9, 3-Amino-2-methoxyquinoline 284461-38-7, N-(5-tert-Butyl-2-methoxyphenyl)-N'-(4-(1,3-dioxoisindolin-5-yloxy)phenyl)urea 284461-48-3 284461-76-3, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-((2-(N-Methylcarbamoyl)-4-pyridyl)oxy)phenyl)urea 284462-29-9 284462-72-2, 3-Chloro-6-(N-acetylamino)-4-(trifluoromethyl)anisole 284462-73-3, 4-Chloro-N-(2-hydroxyethyl)pyridine-2-carboxamide 284462-74-4 284462-76-6 284462-77-7, 5-tert-Butyl-2-methoxyphenyl isocyanate 284462-78-8, 3-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]aniline 284462-79-9, 3-(2-Carbamoyl-4-pyridyloxy)aniline 284462-80-2, 4-(2-Carbamoyl-4-pyridyloxy)aniline 284462-82-4, 4-[[2-(N-Ethylcarbamoyl)-4-pyridyl]oxy]aniline 284462-83-5, 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-3-chloroaniline 284462-85-7, 4-(3-Carbamoylphenoxy)aniline 284462-86-8, 4-[[2-(N,N-Dimethylcarbamoyl)-4-pyridyl]oxy]aniline 284462-87-9 284462-88-0 284462-89-1, 4-[[2-(N-Isopropylcarbamoyl)-4-pyridyl]oxy]aniline 284462-92-6, 3-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-4-methylaniline 284462-93-7, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]aniline 284462-94-8, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]aniline 284462-95-9, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]aniline 284462-96-0 284462-99-3, 4-Chloro-2-methoxy-5-(trifluoromethyl)phenyl isocyanate 284670-99-1, 4-(4-Acetylphenoxy)-5-aminopyridine 284671-00-7, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl)urea 284671-01-8, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea RL: RCT (Reactant); RACT (Reactant or reagent)
- (preparation of  $\omega$ -carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)
- IT 883-62-5P, 3-Methoxy-2-naphthoic acid 13041-60-6P, Methyl 3-methoxy-2-naphthoate 27237-21-4P, 4-(3-Carboxyphenoxy)-1-nitrobenzene 36089-89-1P, 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene 41513-02-4P, 4-Bromo-3-(trifluoromethyl)phenyl isocyanate 50727-06-5P, 5-Hydroxyisindoline-1,3-dione 51727-15-2P, 4-Chloropyridine-2-carbonyl chloride hydrochloride 54579-63-4P, 4-(3-Carboxyphenoxy)aniline

64064-63-7P, 4-[(2-Methylpyridin-5-yl)oxy]-1-nitrobenzene 67291-63-8P,  
 2-Amino-3-methoxynaphthalene 71708-64-0P, 4-[3-(N-Methylcarbamoyl)phenoxy]-1-nitrobenzene 77992-50-8P,  
 4-Bromo-3-(trifluoromethyl)aniline hydrochloride 119431-22-0P,  
 3-Chloro-4-(2,2,2-trifluoroacetyl amino)phenol 153435-79-1P,  
 N-Methyl-3-bromobenzenesulfonamide 176977-85-8P, Methyl  
 4-chloropyridine-2-carboxylate hydrochloride 220000-87-3P,  
 4-Chloro-N-methyl-2-pyridinecarboxamide 228401-15-8P,  
 2-(N-(Benzoyloxycarbonyl)amino)-3-methoxynaphthalene 228401-43-2P,  
 4-(3-Methoxycarbonyl-4-methoxyphenoxy)-1-nitrobenzene 228401-44-3P,  
 4-(3-Carboxy-4-methoxyphenoxy)-1-nitrobenzene 252061-66-8P,  
 5-Hydroxyisoidolin-1-one 284461-73-0P 284461-89-8P  
 284462-37-9P, 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]aniline  
 284462-38-0P, 5-(4-Nitrophenoxy)isoidoline-1,3-dione 284462-39-1P,  
 5-(4-Aminophenoxy)isoidoline-1,3-dione 284462-40-4P,  
 1-(4-tert-Butyl-2-nitrophenyl)-2,5-dimethylpyrrole 284462-41-5P,  
 5-tert-Butyl-2-(2,5-dimethylpyrrolyl)aniline 284462-42-6P,  
 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-2-methylaniline hydrochloride  
 284462-43-7P 284462-44-8P 284462-45-9P, 4-Chloro-2-methoxy-5-(  
 (trifluoromethyl)aniline 284462-46-0P, 4-[3-(N-Methylcarbamoyl)-4-  
 methoxyphenoxy]-1-nitrobenzene 284462-47-1P, 4-[3-(N-Methylcarbamoyl)-4-  
 methoxyphenoxy]aniline 284462-48-2P, 5-(4-Nitrophenoxy)-2-  
 methylisoidoline-1,3-dione 284462-49-3P, 5-(4-Aminophenoxy)-2-  
 methylisoidoline-1,3-dione 284462-51-7P, 4-Chloro-2-[N-(2-morpholin-4-  
 yl)ethyl]carbamoylpyridine 284462-52-8P 284462-53-9P,  
 4-(1-Oxoisoidolin-5-yloxy)-1-nitrobenzene 284462-54-0P,  
 4-(1-Oxoisoidolin-5-yloxy)aniline 284462-55-1P, 4-(3-  
 Ethoxycarbonylphenoxy)-1-nitrobenzene 284462-56-2P, 4-[3-(N-  
 Methylcarbamoyl)phenoxy]aniline 284462-57-3P 284462-58-4P  
 284462-59-5P 284462-60-8P, 4-[3-(N-Methylsulfamoyl)phenoxy]-1-  
 nitrobenzene 284462-61-9P, 4-[3-(N-Methylsulfamoyl)phenoxy]aniline  
 284462-62-0P 284462-63-1P, 4-Chloro-N-[2-(triisopropylsilyloxy)ethyl]pyr-  
 idine-2-carboxamide 284462-64-2P 284462-65-3P, 4-[[2-  
 (Methoxycarbonyl)pyridin-5-yl]oxy]-1-nitrobenzene 284462-66-4P  
 284462-67-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-aminophenyl)Urea  
 284462-68-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-  
 ethoxycarbonylphenyl)Urea 284462-69-7P 284462-70-0P 284462-71-1P  
 284462-84-6P, 4-(4-Methylsulfonylphenoxy)-1-aniline 284462-97-1P  
 284670-98-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of  $\omega$ -carboxy(hetero)aryl substituted di-Ph urea raf  
 kinase inhibitors by reacting arylisocyanates with arylamines)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 62 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:493376 HCAPLUS Full-text

DOCUMENT NUMBER: 133:120155

TITLE: Preparation of  $\omega$ -carboxy aryl substituted  
 diphenyl ureas as p38 kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger,  
 Timothy B.; Scott, William J.; Smith, Roger A.; Wood,  
 Jill E.; Monahan, Mary-Katherine; Natero, Reina;  
 Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 148 pp.

CODEN: PIXXD2

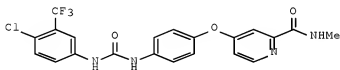
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041698	A1	20000720	WO 2000-US768	20000113 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2359244	A1	20000720	CA 2000-2359244	20000113 <--
EP 1158985	A1	20011205	EP 2000-905597	20000113 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
MX 2001PA07120	A	20011101	MX 2001-PA7120	20010712 <--
US 20030139605	A1	20030724	US 2002-71248	20020211 <--
US 20030105091	A1	20030605	US 2002-86417	20020304 <--
AU 2004200566	A1	20040311	AU 2004-200566	20040213 <--
AU 2004200566	B2	20060817		
AU 2004200722	A1	20040318	AU 2004-200722	20040224 <--
AU 2004200722	B2	20080110		
US 20080027061	A1	20080131	US 2007-845597	20070827 <--
PRIORITY APPLN. INFO.:				
			US 1999-115878P	P 19990113 <--
			US 1999-257265	A2 19990225 <--
			US 1999-425229	A2 19991022 <--
			US 1999-115877P	P 19990113 <--
			US 1999-257266	B2 19990225 <--
			US 1999-425228	B1 19991022 <--
			AU 2000-25016	A3 20000112 <--
			AU 2000-27250	A3 20000113 <--
			WO 2000-US768	W 20000113 <--
			US 2001-948915	A1 20010910 <--
			US 2002-86417	B3 20020304 <--

OTHER SOURCE(S): MARPAT 133:120155  
GI



II

AB The title compds. ADB [I; D = NHCONH; A = substituted moiety of up to 40 carbon atoms of the formula L(ML1)q (wherein L = 5-6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; each of L and L1 contains 0-4 members of the group consisting of N, O and S); B = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the

group consisting of N, O and S], useful in treating p38 mediated diseases, were prepared E.g., a multi-step synthesis of the urea II which showed IC50 of 1-10  $\mu$ M against p38, was given. Compds. I are effective at 0.01-200 mg/kg/day (oral administration).

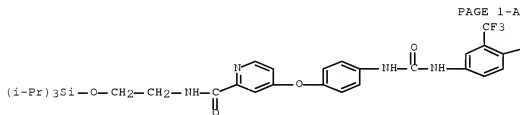
IT 284462-06-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of  $\omega$ -carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

RN 284462-06-2 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (CA INDEX NAME)



IC ICM A61K031-535

ICS A61K031-50; A61K031-445; A61K031-44; A61K031-40; A61K031-34; A61K031-17

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1

IT 284461-86-5P 284461-89-8P 284462-06-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of  $\omega$ -carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P  
 284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P  
 284461-42-3P 284461-43-4P 284461-44-5P  
 284461-45-6P 284461-46-7P 284461-47-8P  
 284461-48-9P 284461-49-0P 284461-50-3E  
 284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P  
 284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P  
 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P  
 284461-63-8P 284461-64-9P 284461-65-0P 284461-66-1P 284461-67-2P  
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284461-73-0P 284461-74-1P 284461-75-2P  
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 284462-17-5P 284462-18-6P 284462-19-7P  
 284462-20-0P 284462-21-1P 284462-22-2P  
 284462-23-3P 284462-24-4P 284462-25-5P 284462-26-6P  
 284462-27-7P 284462-28-8P 284462-29-9P  
 284462-30-2P 284462-31-3P 284462-32-4P  
 284462-33-5P 284462-34-6P 284462-35-7P 284462-36-8P  
 284462-70-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of  $\omega$ -carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 63 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:421667 HCAPLUS Full-text

DOCUMENT NUMBER: 131:58659

TITLE: Preparation of diaryl ureas as inhibitors of p38 kinase.

INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932463	A1	19990701	WO 1998-US27265	19981222 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2315715	A1	19990701	CA 1998-2315715	19981222 <--
AU 9919399	A	19990712	AU 1999-19399	19981222 <--
EP 1042305	A1	20001011	EP 1998-964221	19981222 <--
EP 1042305	B1	20050608		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

JP 2001526276	T	20011218	JP 2000-525400	19981222 <--
JP 3887769	B2	20070228		
AT 297383	T	20050615	AT 1998-964221	19981222 <--
PT 1042305	T	20051031	PT 1998-964221	19981222 <--
ES 2154252	T3	20051201	ES 1998-964221	19981222 <--
EP 1616865	A1	20060118	EP 2005-12144	19981222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
MX 2000PA06227	A	20020311	MX 2000-PA6227	20000622 <--
HK 1032050	A1	20051118	HK 2001-102468	20010407 <--
AU 2003213527	A1	20030814	AU 2003-213527	20030717 <--
PRIORITY APPLN. INFO.:			US 1997-995749	A 19971222 <--
			AU 1999-19399	A3 19981222 <--
			EP 1998-964221	A3 19981222 <--
			WO 1998-US27265	W 19981222 <--

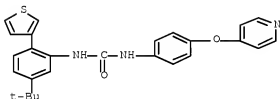
OTHER SOURCE(S): MARPAT 131:58659

AB A method of treating a p-38 mediated disease other than cancer comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl containing  $\geq 1$  6-membered aromatic structure containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuran-2-yl)aniline (preparation given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuran-2-yl)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC50 = 1-10  $\mu$ M.

IT 228399-44-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of diaryl ureas as inhibitors of p38 kinase)

RN 228399-44-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(3-thienyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC	ICM C07D273-00				
	ICS C07D275-00; A61K031-17				
CC	25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)				
	Section cross-reference(s): 1, 27, 28				
IT	370-50-3P	117745-34-3P	228399-32-4P	228399-33-5P	228399-34-6P
	228399-35-7P	228399-38-0P	228399-44-8P	228399-45-9P	
	228399-61-9P	228399-62-0P	228399-63-1P	228399-65-3P	228399-66-4P
	228399-68-6P	228399-69-7P	228399-70-0P	228399-71-1P	228399-72-2P
	228399-74-4P	228399-82-4P	228399-84-6P	228400-63-3P	
	228400-64-4P	228400-65-5P	228400-87-1P	228400-92-8P	228400-93-9P
	228400-94-0P	228400-95-1P	228400-96-2P	228400-97-3P	228400-99-5P
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	228416-64-6P	228416-65-7P	228416-66-8P	228416-67-9P	228416-68-0P



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228418-38-0P	228418-39-1P	228418-40-4P	228418-41-5P	228418-42-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 228399-41-5 228418-48-2 228418-49-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 64 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:421642 HCAPLUS Full-text

DOCUMENT NUMBER: 131:58658

TITLE: Inhibition of raf kinase using symmetrical and unsymmetrical substituted diphenyl ureas

INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez, Mareli; Wang, Ming

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932436	A1	19990701	WO 1998-US26081	19981222 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,			

TR, TT, UA, UG, UZ, VN, YU, ZW  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2315646 A1 19990701 CA 1998-2315646 19981222 <--  
 AU 9919054 A 19990712 AU 1999-19054 19981222 <--  
 AU 763024 B2 20030710  
 EP 1049664 A1 20001108 EP 1998-963809 19981222 <--  
 EP 1049664 B1 20050316

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO

TR 200002616 T2 20001121 TR 2000-2616 19981222 <--  
 TR 200100874 T2 20010621 TR 2001-874 19981222 <--  
 HU 2000004437 A2 20010628 HU 2000-4437 19981222 <--  
 JP 2001526258 T 20011218 JP 2000-525373 19981222 <--  
 BR 9814375 A 20020521 BR 1998-14375 19981222 <--  
 NZ 505843 A 20030630 NZ 1998-505843 19981222 <--  
 EP 1449834 A2 20040825 EP 2003-26051 19981222 <--  
 EP 1449834 A3 20041222

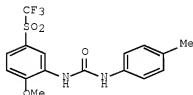
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL

RU 2247109 C2 20050227 RU 2000-120165 19981222 <--  
 AT 291011 T 20050415 AT 1998-963809 19981222 <--  
 ES 2153809 T3 20050716 ES 1998-963809 19981222 <--  
 PL 195808 B1 20071031 PL 1998-342078 19981222 <--  
 NO 2000003230 A 20000821 NO 2000-3230 20000621 <--  
 MX 2000PA06231 A 20020918 MX 2000-PA6231 20000622 <--  
 IN 2000MN00150 A 20050715 IN 2000-MN150 20000704 <--  
 BG 104599 A 20010330 BG 2000-104599 20000712 <--  
 BG 64594 B1 20050831  
 IN 2003MN00960 A 20050429 IN 2003-MN960 20031013 <--

PRIORITY APPLN. INFO.: US 1997-996344 A 19971222 <--  
 EP 1998-963809 A3 19981222 <--  
 WO 1998-US26081 W 19981222 <--

OTHER SOURCE(S): MARPAT 131:58658

GI



II

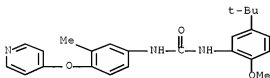
AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepared For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compound II. In an in vitro raf kinase assay, all compds. displayed IC50 values between 1 nM and 10  $\mu$ M.

IT 228399-40-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)

RN 228399-40-4 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[3-methyl-4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07C275-24

ICS C07D213-02; C07D333-02; A61K031-17; A61K031-38; A61K031-44

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 7

IT 370-50-3P 228399-32-4P 228399-33-5P 228399-34-6P 228399-35-7P  
 228399-36-8P 228399-38-0P 228399-39-1P 228399-40-4P  
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 228401-50-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 65 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:591849 BIOSIS Full-text

DOCUMENT NUMBER: PREV200600585463

TITLE: Synthesis of iodine-123 labeled raf kinase inhibitor: A potential SPECT agent.

AUTHOR(S): Kabaika, George W. [Reprint Author]; Mereddy, Arjun R.; Schuller, Hildegard

CORPORATE SOURCE: Univ Tennessee, Dept Chem, Knoxville, TN 37996 USA  
 kabaika@utk.edu; amereddy@mc.utmck.edu

SOURCE: Abstracts of Papers American Chemical Society, (MAR 26 2006) Vol. 231, pp. 309-MEDI.  
 Meeting Info.: 231st National Meeting of the American-Chemical-Society. Atlanta, GA, USA. March 26 -30, 2006. Amer Chem Soc.  
 CODEN: ACSRAL. ISSN: 0065-7727.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Nov 2006  
 Last Updated on STN: 8 Nov 2006

CC General biology - Symposia, transactions and proceedings 00520  
 Enzymes - General and comparative studies: coenzymes 10802  
 Pathology - Diagnostic 12504  
 Pathology - Therapy 12512  
 Respiratory system - Pathology 16006  
 Pharmacology - General 22002  
 Neoplasms - Diagnostic methods 24001  
 Neoplasms - Pathology, clinical aspects and systemic effects 24004  
 Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts  
 Pharmacology; Methods and Techniques; Tumor Biology; Enzymology  
 (Biochemistry and Molecular Biophysics)

IT Diseases  
 lung cancer: respiratory system disease, neoplastic disease, diagnosis, mortality

Lung Neoplasms (MeSH)

IT Chemicals & Biochemicals  
 BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; iodine-123;  
 raf kinase inhibitor; BAY 43-9006  
 radioiodinated analogue: antineoplastic-drug

IT Methods & Equipment  
 SPECT imaging [single photon emission computed tomography imaging]:  
 laboratory techniques, diagnostic techniques, clinical techniques,  
 imaging and microscopy techniques

GT USA (North America, Nearctic region)

RN 284461-73-0 (BAY 43-9006)  
 15715-08-9 (iodine-123)

L110 ANSWER 66 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2006:663269 BIOSIS Full-text

DOCUMENT NUMBER: PREV200600657401

TITLE: Sorafenib for the treatment of renal cell carcinoma.

AUTHOR(S): Hughes, Caren L. [Reprint Author]; Tan, Winston W.;  
Ferrone, Marcus

CORPORATE SOURCE: Univ Texas, MD Anderson Canc Ctr, Div Pharm, Unit 90, 1515  
Holcombe Blvd, Houston, TX 77030 USA  
calhughes@mdanderson.com

SOURCE: Journal of Pharmacy Technology, (SEP-OCT 2006) Vol. 22, No.  
5, pp. 281-288.

CODEN: JPTEEB. ISSN: 8755-1225.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Nov 2006

Last Updated on STN: 29 Nov 2006

AB Objective: To summarize the pharmacology, development, and clinical application of sorafenib, a specific tyrosine kinase and vascular growth factor inhibitor, for the treatment of renal cell carcinoma (RCC).Data Sources: Clinical literature, including both primary studies and review articles, was obtained by searching MEDLINE (1966-May 2006), using the search terms BAY 43-9006, sorafenib, renal cell carcinoma, and tyrosine kinase inhibitor. Additional information was supplied by the manufacturer, Bayer HealthCare Pharmaceuticals.Study Selection and Data Extraction: Review articles, abstracts, and clinical studies related to sorafenib were analyzed. An evaluation of the research exploring sorafenib as a potential therapy for RCC was conducted. Relevant information was then selected and is reviewed in this article.Data Synthesis: Knowledge of the cellular abnormalities that can cause solid tumors has led to the development of medications that block these pathways. Sorafenib is an oral tyrosine kinase inhibitor that both blocks the Raf kinase pathway and inhibits vascular growth factors. Phase I and II trials have demonstrated that sorafenib has activity against RCC. Dermatologic reactions (rash, desquamation), fatigue, and hypertension have been the most commonly seen treatment-related adverse events. Sorafenib received FDA approval in December 2005 for treatment of advanced RCC.Conclusions: Sorafenib is a novel oral tyrosine kinase inhibitor effective in the treatment of RCC.

CC Cytology - Animal 02506

Cytology - Human 02508

Enzymes - General and comparative studies: coenzymes 10802

Pathology - Therapy 12512

Urinary system - Physiology and biochemistry 15504

Urinary system - Pathology 15506

Pharmacology - General 22002

Pharmacology - Clinical pharmacology 22005

Toxicology - Pharmacology 22504

Neoplasms - Pathology, clinical aspects and systemic effects 24004

Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts

Pharmacology; Oncology (Human Medicine, Medical Sciences); Urology  
(Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms

renal cell: excretory system

IT Diseases

renal cell carcinoma: urologic disease, neoplastic disease, drug  
therapy

Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH)

IT Chemicals & Biochemicals

tyrosine kinase; vascular growth factor; BAY

43-9006: antineoplastic-drug; sorafenib: antineoplastic-drug, enzyme

inhibitor-drug, dosage, adverse effect, pharmacokinetics, Beyer  
Healthcare Pharmaceuticals, phase II clinical trial, phase I clinical  
trial

## ORGN Classifier

Hominidae 86215

## Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

## Organism Name

human (common)

## Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 80449-02-1 (tyrosine kinase)

284461-73-0 (BAY 43-9006)

L110 ANSWER 67 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2006:42184 BIOSIS [Full-text](#)

DOCUMENT NUMBER: PREV200600031990

TITLE: Targeted agents for the treatment of advanced renal cell  
carcinoma.

AUTHOR(S): Stadler, Walter M. [Reprint Author]

CORPORATE SOURCE: Univ Chicago, Div Genitourinary Oncol, Hematol Oncol Sect,  
Dept Med, Chicago, IL 60637 USA  
wstadler@medicine.bsd.uchicago.edu

SOURCE: Cancer, (DEC 1 2005) Vol. 104, No. 11, pp. 2323-2333.  
CODEN: CANCAR. ISSN: 0008-543X.

DOCUMENT TYPE: Article

General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 28 Dec 2005

Last Updated on STN: 28 Dec 2005

AB Metastatic renal cell carcinoma (RCC) is currently one of the most treatment-resistant malignancies. However, the elucidation of the molecular mechanisms underlying RCC development has led to the identification of promising targets for novel therapeutic agents. The involvement of the Von Hippel-Lindau protein pathway in clear cell RCC suggests that downstream targets of this pathway, namely, signaling through vascular endothelial growth factor (VEGF) in endothelial cells, platelet-derived growth factor (PDGF) in endothelial cells and pericytes, and the epidermal growth factor receptor (EGFR) pathway in tumor cells are all reasonable and rational therapeutic targets. A number of agents are in development that target VEGF (bevacizumab, a recombinant, humanized monoclonal antibody) or its receptor, VEGFR (PTK787, SU011248, and BAY 43-9006, all of which are small molecule inhibitors). Agents targeting EGFR also are being investigated clinically (gefitinib, cetuximab, erlotinib, and ABX-EGF). The Raf/MEK/ERK pathway is an important downstream convergence point for signaling through VEGFR, platelet-derived growth factor receptor (PDGFR), and EGFR (all have receptor tyrosine kinase activity) and also has important antiapoptotic effects, thereby providing an attractive target for intervention. In addition to inhibiting VEGFR and PDGFR-mediated angiogenic pathways, BAY 43-9006 has been shown to inhibit the Raf/MEK/ERK pathway at the level of Raf kinase. MEK-directed therapeutic approaches are also in development. Given that multiple molecular pathways are implicated in tumor cell growth, antitumor activity may be increased by using individual agents that target multiple pathways, or by combining different agents to allow vertical or horizontal inhibition of relevant pathways.

CC Cytology - Animal 02506

Cytology - Human 02508

Biochemistry studies - Proteins, peptides and amino acids 10064

Enzymes - General and comparative studies: coenzymes 10802

Pathology - General 12502

Pathology - Therapy 12512  
 Urinary system - Physiology and biochemistry 15504  
 Urinary system - Pathology 15506  
 Endocrine - General 17002  
 Pharmacology - General 22002  
 Pharmacology - Clinical pharmacology 22005  
 Pharmacology - Urinary system 22032  
 Neoplasms - Pathology, clinical aspects and systemic effects 24004  
 Neoplasms - Therapeutic agents and therapy 24008  
 IT Major Concepts  
     Pharmacology; Enzymology (Biochemistry and Molecular Biophysics);  
     Oncology (Human Medicine, Medical Sciences); Nephrology (Human  
     Medicine, Medical Sciences)  
 IT Parts, Structures, & Systems of Organisms  
     renal cell: excretory system; endothelial cell: excretory system;  
     pericyte: excretory system  
 IT Diseases  
     metastatic renal cell carcinoma: urologic disease, neoplastic disease,  
     drug therapy, pathology  
     Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH); Neoplasm  
     Metastasis (MeSH)  
 IT Chemicals & Biochemicals  
     Raf kinase [EC 2.7.1.37]; vascular endothelial  
     growth factor [VEGF]; Raf; extracellular regulated kinase [ERK];  
     mitogen activated protein kinase kinase [MEK] [EC 2.7.1.37];  
     bevacizumab: antineoplastic-drug, renal-acting-drug; PTK787;  
     antineoplastic-drug, renal-acting-drug; gefitinib: antineoplastic-drug,  
     renal-acting-drug; cetuximab: antineoplastic-drug, renal-acting-drug;  
     erlotinib: antineoplastic-drug, renal-acting-drug; platelet-derived  
     growth factor receptor [PDGFR]: antiapoptotic effect; epidermal growth  
     factor receptor [EGFR]: antiapoptotic effect; vascular endothelial  
     growth factor receptor [VEGFR]: antiapoptotic effect; SU011248;  
     antineoplastic-drug, renal-acting-drug; BAY 43-9006;  
     antineoplastic-drug, renal-acting-drug, enzyme inhibitor-drug;  
     ABX-epidermal growth factor receptor [ABX-EGF]: antineoplastic-drug,  
     renal-acting-drug  
 IT Miscellaneous Descriptors  
     angiogenesis  
 ORGN Classifier  
     Hominidae 86215  
     Super Taxa  
         Primates; Mammalia; Vertebrata; Chordata; Animalia  
     Organism Name  
         human (common)  
     Taxa Notes  
         Animals, Chordates, Humans, Mammals, Primates, Vertebrates  
 RN 144378-33-6 (Raf kinase)  
     144378-33-6 (EC 2.7.1.37)  
     127464-60-2 (vascular endothelial growth factor)  
     127464-60-2 (VEGF)  
     142805-58-1 (mitogen activated protein kinase kinase)  
     142805-58-1 (MEK)  
     142805-58-1 (EC 2.7.1.37)  
     216974-75-3 (bevacizumab)  
     212142-18-2 (PTK787)  
     184475-35-2 (gefitinib)  
     205923-56-4 (cetuximab)  
     183321-74-6 (erlotinib)  
     284461-73-0 (BAY 43-9006)

L110 ANSWER 68 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on  
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ACCESSION NUMBER: 2007:264012 BIOSIS Full-text  
DOCUMENT NUMBER: PREV200700274079

TITLE: BAY 43-9006 (sorafenib) is a potent inhibitor of FLT3  
tyrosine kinase signaling and  
proliferation in AML cells.

AUTHOR(S): Auclair, Daniel [Reprint Author]; Miller, Donna; Carter,  
Christopher; Chang, Yong; Polony, Barbara; Zhang, Xiaomei;  
Yatsula, Victoria; Pickett, Walter; Housley, Timothy; Burd,  
Amy; Shi, Hong; Rocks, Sandy; Gedrich, Richard; Abriola,  
Laura; Apanovitch, Don; Enyedy, Istvan; Dumas, Jacques;  
Riedl, Bernd; Trail, Pamela A.; Wilhelm, Scott M.

CORPORATE SOURCE: Bayer Healthcare Pharmaceut, West Haven, CT USA  
SOURCE: Proceedings of the American Association for Cancer Research  
Annual Meeting, (APR 2005) Vol. 46, pp. 1409.  
Meeting Info.: 96th Annual Meeting of the  
American-Association-for-Cancer-Research. Anaheim, CA, USA.  
April 16 -20, 2005. Amer Assoc Canc Res.  
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Apr 2007  
Last Updated on STN: 11 Jul 2007

CC General biology - Symposia, transactions and proceedings 00520  
Cytology - Animal 02506  
Cytology - Human 02508  
Enzymes - General and comparative studies: coenzymes 10802  
Pathology - Therapy 12512  
Blood - Blood and lymph studies 15002  
Blood - Blood cell studies 15004  
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Neoplasms - Therapeutic agents and therapy 24008  
Neoplasms - Blood and reticuloendothelial neoplasms 24010

IT Major Concepts  
Pharmacology; Blood and Lymphatics (Transport and Circulation);  
Enzymology (Biochemistry and Molecular Biophysics); Tumor Biology

IT Parts, Structures, & Systems of Organisms  
blood: blood and lymphatics

IT Diseases  
acute myeloid leukemia: neoplastic disease, blood and lymphatic disease  
Leukemia, Myeloid (MeSH)

IT Chemicals & Biochemicals  
ERK1/2; Stat5; RAF kinase; VEGFR [vascular  
endothelial growth factor receptor]; FLT3 tyrosine  
kinase: signaling; BAY 43-9006 [Sorafenib]:  
antineoplastic-drug, enzyme inhibitor-drug

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
MV4-11 cell line (cell\_line)  
HEK-293 cell line (cell\_line)  
RS4-11 cell line (cell\_line)  
EOL-1 cell line (cell\_line)



Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier  
 Muridae 86375  
 Super Taxa  
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name  
 mouse (common)

Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,  
 Rodents, Vertebrates

RN 144378-33-6 (RAF kinase)  
 284461-73-0 (BAY 43-9006)  
 284461-73-0 (Sorafenib)

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ACCESSION NUMBER: 2005:258211 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200510048678  
 TITLE: Raf kinase as a target for anticancer  
 therapeutics.

AUTHOR(S): Sridhar, Srikala S.; Hedley, David; Siu, Lillian L.  
 [Reprint Author]

CORPORATE SOURCE: Univ Hlth Network, Princess Margaret Hosp, Dept Med Oncol  
 and Hematol, 610 Univ Ave, Suite 5-210, Toronto, ON M5G 2M9,  
 Canada  
 lillian.siu@uhn.on.ca

SOURCE: Molecular Cancer Therapeutics, (APR 2005) Vol. 4, No. 4,  
 pp. 677-685.  
 ISSN: 1535-7163.

DOCUMENT TYPE: Article  
 General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Jul 2005  
 Last Updated on STN: 14 Jul 2005

AB The Ras-Raf-MEK-ERK (ERK) pathway is a logical therapeutic target because it  
 represents a common downstream pathway for several key growth factor tyrosine  
 kinase receptors, which are often mutated or overexpressed in human cancers.  
 Although considered mainly growth-promoting, in certain contexts, this pathway  
 also seems to be apoptosis-suppressing. Several novel agents targeting this  
 pathway have now been developed and are in clinical trials. One of the most  
 interesting new agents is BAY 43-9006. Although initially developed as a Raf  
 kinase inhibitor, it can also target several other important tyrosine kinases  
 including VEGFR-2, Flt-3, and c-Kit, which contributes to its  
 antiproliferative and antiangiogenic properties. To date, encouraging results  
 have been seen with BAY 43-9006, particularly in renal cell cancers which are  
 highly vascular tumors. This review will provide an overview of the ERK  
 signaling pathway in normal and neoplastic tissue, with a specific focus on  
 novel therapies targeting the ERK pathway at the level of Raf kinase.

CC Pathology - Therapy 12512  
 Urinary system - Pathology 15506  
 Pharmacology - General 22002  
 Pharmacology - Clinical pharmacology 22005  
 Neoplasms - Pathology, clinical aspects and systemic effects 24004  
 Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts  
 Pharmacology; Oncology (Human Medicine, Medical Sciences); Urology  
 (Human Medicine, Medical Sciences)

IT Diseases  
 renal cancer: urologic disease, neoplastic disease, drug therapy

Kidney Neoplasms (MeSH)

IT Chemicals & Biochemicals  
 Raf kinase [EC 2.7.1.37]; BAY 43-9006:  
 antineoplastic-drug, enzyme inhibitor-drug; VEGFR-2 kinase; Fit-3  
 kinase; c-Kit kinase

ORGN Classifier  
 Hominidae 86215  
 Super Taxa  
 Primates; Mammalia; Vertebrata; Chordata; Animalia  
 Organism Name  
 human (common)  
 Taxa Notes  
 Animals, Chordates, Humans, Mammals, Primates, Vertebrate

RN 144378-33-6 (Raf kinase)  
 144378-33-6 (EC 2.7.1.37)  
 284463-73-0 (BAY 43-9006)  
 218925-58-7 (VEGFR-2 kinase)  
 138359-29-2 (c-Kit kinase)

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ACCESSION NUMBER: 2005:185218 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV200500186216  
 TITLE: The Raf kinase inhibitor BAY  
 43-9006 reduces cellular uptake of platinum compounds and  
 cytotoxicity in human colorectal carcinoma cell lines.

AUTHOR(S): Heim, Martina; Scharifi, Mariam; Zisowsky, Jochen; Jaehde,  
 Ulrich; Voliotis, Dimitris; Seeber, Siegfried; Strumberg,  
 Dirk [Reprint Author]

CORPORATE SOURCE: Sch MedDept Hematol and Med Oncol, Ruhr Univ Bochum,  
 Hoeskeskampring 40, D-44621, Herne, Germany  
 dirk.strumberg@uni-essen.de

SOURCE: Anti-Cancer Drugs, (February 2005) Vol. 16, No. 2, pp.  
 129-136, print.  
 CODEN: ANTDEV. ISSN: 0959-4973.

DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 18 May 2005  
 Last Updated on STN: 18 May 2005

AB Raf kinase plays a central role in oncogenic signaling and acts as a  
 downstream effector of Ras in the extracellular signal-regulated (ERK) kinase  
 pathway. BAY 43-9006 (BAY) is a novel signal transduction inhibitor that  
 prevents tumor cell proliferation and angiogenesis through blockade of the  
 Raf/MEK/ERK pathway at the level of Raf kinase and the receptor tyrosine  
 kinases vascular endothelial growth factor receptor-2 and platelet-derived  
 growth factor receptor-beta. The present study evaluates the effects of  
 combining BAY and platinum derivatives on human colorectal cancer cells using  
 different incubation protocols. Our data show that the combination of  
 oxaliplatin or cisplatin with BAY results in marked antagonism irrespective of  
 the used application schedule. Furthermore, BAY abrogates the cisplatin-  
 induced G2 arrest as well as the G1 arrest induced by oxaliplatin. BAY alone  
 arrests cancer cells in their current cell cycle phase and affects cell cycle  
 regulative genes. Specifically, BAY reduced the protein expression of p21Cip1  
 as well as cyclin D1, and inhibits the expression of cdc2 (cdk1). Utilizing  
 atom absorption spectrometry, BAY significantly reduced cellular uptake of  
 platinum compounds and thereby the generation of DNA adducts. Taken together,  
 co-incubation with BAY results in reduced cellular uptake of platinum  
 compounds and consecutively reduced generation of DNA adducts, and eventually  
 decreased cellular cytotoxicity in human colorectal cancer cells. Our results  
 indicate that the Raf kinase inhibitor BAY 43-9006 might also directly or

indirectly interact with platinum transporter proteins in vitro. Copyright  
2005 Lippincott Williams & Wilkins.

CC Genetics - General 03502  
Genetics - Human 03508  
Biochemistry studies - General 10060  
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biochemistry studies - Minerals 10069  
Enzymes - General and comparative studies: coenzymes 10802  
Pathology - Therapy 12512  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts  
Molecular Genetics (Biochemistry and Molecular Biophysics);  
Pharmacology; Tumor Biology

IT Chemicals & Biochemicals  
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; DNA; Mek;  
Raf kinase [EC 2.7.1.37]; cdc2; cisplatin:  
antineoplastic-drug; cyclin D1; extracellular signal-regulated kinase  
[EC 2.7.1.37]; oxaliplatin: antineoplastic-drug; p21Cip1;  
platelet-derived growth factor receptor-beta; platinum; vascular  
endothelial growth factor receptor-2

IT Methods & Equipment  
atom absorption spectrometry: laboratory techniques, spectrum analysis  
techniques

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
HCT8 cell line (cell line): human colon carcinoma cells  
HT 29 cell line (cell line): human colon carcinoma cells  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 264461-73-6 (BAY 43-9006)  
144378-33-6 (Raf kinase)  
9026-43-1 (Raf kinase)  
144378-33-6 (EC 2.7.1.37)  
9026-43-1 (EC 2.7.1.37)  
15663-27-1 (cisplatin)  
142243-02-5 (extracellular signal-regulated kinase)  
9026-43-1 (extracellular signal-regulated kinase)  
142243-02-5 (EC 2.7.1.37)  
9026-43-1 (EC 2.7.1.37)  
61825-94-3 (oxaliplatin)  
7440-06-4 (platinum)

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ACCESSION NUMBER: 2005:32325 BIOSIS [Full-text](#)  
DOCUMENT NUMBER: PREV200500030385  
TITLE: BAY 43-9006 exhibits broad spectrum oral antitumor activity  
and targets the RAF/MEK/ERK pathway and receptor  
tyrosine kinases involved in tumor  
progression and angiogenesis.

AUTHOR(S): Wilhelm, Scott M. [Reprint Author]; Carter, Christopher;  
Tang, Liya; Wilkie, Dean; McNabola, Angela; Rong, Hong;  
Chen, Charles; Zhang, Xiaomei; Vincent, Patrick; McHugh,

Mark; Cao, Yichen; Shujath, Jaleel; Gawlak, Susan; Eveleigh, Deepa; Rowley, Bruce; Liu, Li; Adnane, Lila; Lynch, Mark; Auclair, Daniel; Taylor, Ian; Gedrich, Rich; Voznesensky, Andrei; Riedl, Bernd; Post, Leonard E.; Bollag, Gideon; Trail, Pamela A.

CORPORATE SOURCE: Dept Canc Res, Bayer Pharmaceut Corp, 400 Morgan Lane, W Haven, CT, 06516, USA

scott.wilhelm.b@bayer.com  
SOURCE: Cancer Research, (October 1 2004) Vol. 64, No. 19, pp. 7099-7109. print.  
ISSN: 0008-5472 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Jan 2005

Last Updated on STN: 12 Jan 2005

AB The RAS/RAF signaling pathway is an important mediator of tumor cell proliferation and angiogenesis. The novel bi-aryl urea BAY 43-9006 is a potent inhibitor of Raf-1, a member of the RAF/MEK/ERK signaling pathway. Additional characterization showed that BAY 43-9006 suppresses both wild-type and V599E mutant BRAF activity in vitro. In addition, BAY 43-9006 demonstrated significant activity against several receptor tyrosine kinases involved in neovascularization and tumor progression, including vascular endothelial growth factor receptor (VEGFR)-2, VEGFR-3, platelet-derived growth factor receptor beta, Flt-3, and c-KIT. In cellular mechanistic assays, BAY 43-9006 demonstrated inhibition of the mitogen-activated protein kinase pathway in colon, pancreatic, and breast tumor cell lines expressing mutant KRAS or wild-type or mutant BRAF, whereas non-small-cell lung cancer cell lines expressing mutant KRAS were insensitive to inhibition of the mitogen-activated protein kinase pathway by BAY 43-9006. Potent inhibition of VEGFR-2, platelet-derived growth factor receptor P, and VEGFR-3 cellular receptor autophosphorylation was also observed for BAY 43-9006. Once daily oral dosing of BAY 43-9006 demonstrated broad-spectrum antitumor activity in colon, breast, and non-small-cell lung cancer xenograft models. Immunohistochemistry demonstrated a close association between inhibition of tumor growth and inhibition of the extracellular signal-regulated kinases (ERKs) 1/2 phosphorylation in two of three xenograft models examined, consistent with inhibition of the RAF/MEK/ERK pathway in some but not all models. Additional analyses of microvessel density and microvessel area in the same tumor sections using antimurine CD31 antibodies demonstrated significant inhibition of neovascularization in all three of the xenograft models. These data demonstrate that BAY 43-9006 is a novel dual action RAF kinase and VEGFR inhibitor that targets tumor cell proliferation and tumor angiogenesis.

CC Cytology - General 02502  
Cytology - Animal 02506  
Cytology - Human 02508  
Biochemistry studies - General 10060  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Pathology - Therapy 12512  
Digestive system - Pathology 14006  
Respiratory system - Pathology 16006  
Reproductive system - Pathology 16506  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts  
Biochemistry and Molecular Biophysics; Cell Biology; Oncology (Human Medicine, Medical Sciences); Pharmacology

IT Diseases  
breast cancer: neoplastic disease, reproductive system disease/female

Breast Neoplasms (MeSH)

IT Diseases  
colon cancer: digestive system disease, neoplastic disease  
Colonic Neoplasms (MeSH)

IT Diseases  
non-small-cell lung cancer: neoplastic disease, respiratory system disease  
Carcinoma, Non-Small-Cell Lung (MeSH); Lung Neoplasms (MeSH)

IT Diseases  
pancreatic cancer: digestive system disease, neoplastic disease  
Pancreatic Neoplasms (MeSH)

IT Chemicals & Biochemicals  
BRAF protein; Bay 43-9006: antineoplastic-drug, oral administration;  
CD31 antibody; Flt-3; MEK/ERK; RAF; RAS; Raf-1 [EC 2.7.1.37]; c-KIT;  
mitogen-activated protein kinase pathway; platelet-derived growth  
factor receptor beta; receptor tyrosine kinase [EC  
2.7.1.112]; vascular endothelial growth factor receptor 2 [VEGFR-2];  
vascular endothelial growth factor receptor 3 [VEGFR-3]

IT Methods & Equipment  
cellular mechanistic assay: bioassay techniques, laboratory techniques;  
immunochimistry: immunologic techniques, laboratory techniques

IT Miscellaneous Descriptors  
RAF/MEK/ERK signaling pathway; angiogenesis; tumor progression

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
BxPC-3 cell line (cell line)  
HASMC cell line (cell line)  
HEK-293 cell line (cell line)  
HUVEC cell line (cell line)  
LOX cell line (cell line)  
MDA-MB-231 cell line (cell line)  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
NIH 3T3 cell line (cell line)  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,  
Rodents, Vertebrates

RN 284461-73-6 (Bay 43-9006)  
9026-43-1 (Raf-1)  
9026-43-1 (EC 2.7.1.37)  
340830-03-7 (receptor tyrosine kinase)  
80449-02-1 (receptor tyrosine kinase)  
340830-03-7 (EC 2.7.1.112)  
80449-02-1 (EC 2.7.1.112)

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ACCESSION NUMBER: 2004:391335 BIOSIS [Full-text](#)

DOCUMENT NUMBER: PREV200400393629

TITLE: Validation of a liquid chromatography assay for the  
quantification of the Raf Kinase  
inhibitor BAY 43-9006 in small volumes of mouse

serum.

AUTHOR(S): Afify, Samar; Rapp, Ulf R.; Hogger, Petra [Reprint Author]

CORPORATE SOURCE: Inst Pharm und Lebensmittelchem, Univ Wurzburg, Am Hubland, D-97074, Wurzburg, Germany  
hogger@pzc.uni-wuerzburg.de

SOURCE: Journal of Chromatography B, (September 25 2004) Vol. 809, No. 1, pp. 99-103. print.  
ISSN: 1570-0232 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 6 Oct 2004  
Last Updated on STN: 6 Oct 2004

AB BAY 43-9006 is a selective Raf-1 kinase inhibitor with antitumor activity against a variety of human cancers. A highly sensitive HPLC method for determination of BAY 43-9006 in small volumes of serum (30 µl) was developed. Sample preparation involved a liquid-liquid extraction procedure with tolinaftate as internal standard followed by linear gradient elution at a reversed phase C18 column and UV detection. The method was selective and the calibration curves were linear over the concentration range of 80-2000 ng/ml. The intra-day accuracy ranged from 99.9 to 107.6% and the inter-day accuracy from 94.6 to 115%. The lower limit of quantitation (LOQ) was 80 ng/ml with an accuracy of 105.8%. Thus, this method has been validated and can be applied for the drug monitoring or pharmacokinetic studies of BAY 43-9006 in small volumes of serum samples. Copyright 2004 Elsevier B.V. All rights reserved.

CC Pathology - Therapy 12512  
Blood - Blood and lymph studies 15002  
Blood - Blood cell studies 15004  
Pharmacology - General 22002  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts  
Methods and Techniques; Pharmacology

IT Parts, Structures, & Systems of Organisms  
serum: blood and lymphatics, small volumes

IT Diseases  
cancer: neoplastic disease, drug therapy  
Neoplasms (MeSH)

IT Chemicals & Biochemicals  
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug, selective  
Raf-1 kinase inhibitor; tolinaftate: internal standard

IT Methods & Equipment  
UV detection: laboratory techniques, spectrum analysis techniques;  
linear gradient elution: laboratory techniques; liquid chromatography:  
chromatographic techniques, laboratory techniques; liquid-liquid  
extraction: laboratory techniques; reversed phase C-18 column:  
laboratory equipment

IT Miscellaneous Descriptors  
calibration curves; inter-day accuracy; intra-day accuracy; lower limit  
of quantitation [LOQ]

ORGN Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
mouse (common)  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,  
Rodents, Vertebrates

RN ES4461-73-0 (BAY 43-9006)  
2398-96-1 (tolinaftate)

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ACCESSION NUMBER: 2003189385 EMBASE Full-text  
 TITLE: Clinical review 158 - Beyond radioiodine: A review of potential new therapeutic approaches for thyroid cancer.  
 AUTHOR: Braga-Basaria, Milena; Ringel, Matthew D., Dr. (correspondence)  
 CORPORATE SOURCE: Washington Hospital Center, MedStar Research Institute, Washington, DC 20010, United States. matthew.ringel@medstar.net  
 AUTHOR: Braga-Basaria, Milena  
 CORPORATE SOURCE: SEMPR, Servico de Endocrinol. e Metabologia, Univ. Federal do Parana, Curitiba 80.060-240, Brazil.  
 AUTHOR: Ringel, Matthew D., Dr. (correspondence)  
 CORPORATE SOURCE: 110 Irving Street NW, Washington, DC 20010, United States. matthew.ringel@medstar.net  
 AUTHOR: Ringel, Matthew D., Dr. (correspondence)  
 CORPORATE SOURCE: 110 Irving Street NW, Washington, DC 20010, United States. matthew.ringel@medstar.net  
 SOURCE: Journal of Clinical Endocrinology and Metabolism, (1 May 2003) Vol. 88, No. 5, pp. 1947-1960.  
 Refs: 104  
 ISSN: 0021-972X CODEN: JCEMAZ  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 016 Cancer  
 003 Endocrinology  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 29 May 2003  
 Last Updated on STN: 29 May 2003

AB One of the greatest challenges in the management of patients with follicular cell-derived thyroid cancer is the treatment of tumors that progress despite surgery, radioiodine, and T(4) suppression of TSH. As knowledge of thyroid cancer biology improves, the potential exists to develop compounds targeted to treat thyroid cancers that do not respond to traditional therapy. Recently, the development of therapies targeted against specific molecular pathways involved in cancer progression has resulted in dramatic responses in patients with chronic myelogenous leukemia, gastrointestinal stromal tumors, and other cancers. A number of compounds are currently being evaluated in clinical trials that alter pathways involved thyroid cancer, and several of these agents have been tested in thyroid cancer in vitro and in vivo. In this review we will discuss the mechanisms of action and preclinical/clinical data for several of these compounds that have the potential to play an important role in the management of thyroid cancer in the future.

CT Medical Descriptors:  
 breast carcinoma: DT, drug therapy  
 cancer radiotherapy  
 clinical trial  
 colon carcinoma: DT, drug therapy  
 colorectal carcinoma: DT, drug therapy  
 drug activity  
 drug effect  
 drug receptor binding  
 gene activation  
 gene function

gene mutation  
 head and neck carcinoma: DT, drug therapy  
 head and neck carcinoma: RT, radiotherapy  
 hematologic malignancy: DT, drug therapy  
 human  
 lung carcinoma: DT, drug therapy  
 nonhuman  
 pancreas carcinoma: DT, drug therapy  
 priority journal  
 prostate carcinoma: DT, drug therapy  
 protein expression  
 review  
 side effect: SI, side effect  
 solid tumor: DT, drug therapy  
 \*thyroid carcinoma: DT, drug therapy  
 \*thyroid carcinoma: ET, etiology  
 urinary tract carcinoma: DT, drug therapy

CT

Drug Descriptors:  
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: AE, adverse drug reaction  
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: CT, clinical trial  
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: DT, drug therapy  
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: PO, oral drug administration  
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonfyl) 1h 1,4 benzodiazepine: CT, clinical trial  
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonfyl) 1h 1,4 benzodiazepine: CB, drug combination  
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonfyl) 1h 1,4 benzodiazepine: DT, drug therapy  
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonfyl) 1h 1,4 benzodiazepine: PD, pharmacology  
 \*antisense oligonucleotide: AE, adverse drug reaction  
 \*antisense oligonucleotide: CT, clinical trial  
 \*antisense oligonucleotide: CB, drug combination  
 \*antisense oligonucleotide: DT, drug therapy  
 \*antisense oligonucleotide: PD, pharmacology  
 bevacizumab: AE, adverse drug reaction  
 bevacizumab: CT, clinical trial  
 bevacizumab: DT, drug therapy  
 bevacizumab: PD, pharmacology  
 cgp 69846a: AE, adverse drug reaction  
 cgp 69846a: CT, clinical trial  
 cgp 69846a: DT, drug therapy  
 cgp 69846a: PD, pharmacology  
 cisplatin: CB, drug combination  
 cisplatin: DT, drug therapy  
 doxorubicin: CB, drug combination  
 doxorubicin: DT, drug therapy  
 epidermal growth factor receptor: EC, endogenous compound  
 epidermal growth factor receptor antibody: CT, clinical trial  
 epidermal growth factor receptor antibody: DT, drug therapy  
 epidermal growth factor receptor antibody: PD, pharmacology  
 gemcitabine: CB, drug combination  
 gemcitabine: DT, drug therapy  
 isis 2503: AE, adverse drug reaction  
 isis 2503: CT, clinical trial  
 isis 2503: CB, drug combination



isis 2503: DT, drug therapy  
 isis 2503: PD, pharmacology  
 l 778123: AE, adverse drug reaction  
 l 778123: CT, clinical trial  
 lonafarnib: AE, adverse drug reaction  
 lonafarnib: CT, clinical trial  
 lonafarnib: CB, drug combination  
 lonafarnib: DT, drug therapy  
 manumycin: CB, drug combination  
 manumycin: DT, drug therapy  
 manumycin: PD, pharmacology  
 mitogen activated protein kinase inhibitor: AE, adverse drug reaction  
 mitogen activated protein kinase inhibitor: CT, clinical trial  
 mitogen activated protein kinase inhibitor: DT, drug therapy  
 mitogen activated protein kinase inhibitor: PO, oral drug administration  
 paclitaxel: CB, drug combination  
 paclitaxel: DT, drug therapy  
 paclitaxel: PD, pharmacology  
 phenylacetic acid: AE, adverse drug reaction  
 phenylacetic acid: CT, clinical trial  
 phenylacetic acid: IV, intravenous drug administration  
 phenylacetic acid: PD, pharmacology  
 phosphotransferase inhibitor: AE, adverse drug reaction  
 phosphotransferase inhibitor: CT, clinical trial  
 phosphotransferase inhibitor: DT, drug therapy  
 phosphotransferase inhibitor: PD, pharmacology  
 protein antibody  
 protein farnesyltransferase inhibitor: CT, clinical trial  
 \*radioactive iodine: DT, drug therapy  
 Ras protein: EC, endogenous compound  
 semaxanib: DT, drug therapy  
 semaxanib: PD, pharmacology  
 sorafenib  
 tipifarnib: CT, clinical trial  
 tipifarnib: CB, drug combination  
 tipifarnib: DT, drug therapy  
 topotecan: CB, drug combination  
 topotecan: DT, drug therapy  
 trastuzumab: CT, clinical trial  
 trastuzumab: CB, drug combination  
 trastuzumab: DT, drug therapy  
 trastuzumab: PD, pharmacology  
 tyrosine kinase receptor: EC, endogenous compound  
 unindexed drug  
 vasculotropin antibody: AE, adverse drug reaction  
 vasculotropin antibody: CT, clinical trial  
 vasculotropin antibody: DT, drug therapy  
 vasculotropin antibody: PD, pharmacology  
 vasculotropin receptor: EC, endogenous compound  
 (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide)  
 212631-79-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4  
 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9,  
 195987-41-8; (bevacizumab) 216974-75-3; (cgp 69846a) 177075-18-2;  
 (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (doxorubicin) 23214-92-8,  
 25316-40-9; (gemcitabine) 103882-84-4; (isis 2503) 149957-14-2;  
 (lonafarnib) 193275-84-2; (manumycin) 52665-74-4; (paclitaxel) 33069-62-4;  
 (phenylacetic acid) 103-82-2; (semaxanib) 186610-95-7; (sorafenib)  
 284461-73-0; (tipifarnib) 192185-72-1; (topotecan) 119413-54-6,  
 123948-87-8; (trastuzumab) 180288-69-1; (vasculotropin receptor)  
 301253-48-5

RN

CN (1) avastin; (2) isis 2503; (3) isis 5132; (4) l 778123; (5) lonafarnib;  
(6) semaxanib; (7) tipifarnib; (8) trastuzumab; bay 439006; bms 214662; pd  
184352

CO (1) Genentech (United States); (2) Isis (United States); (3) Isis; (4)  
Merck and Co (United States); (5) Schering Plough (United States); (6)  
Sugen (United States); (7) Johnson and Johnson (United States); (8)  
Genentech

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ACCESSION NUMBER: 2003455328 EMBASE Full-text  
TITLE: Tyrosine Kinase Inhibitors as Cancer  
Therapy.

AUTHOR: Nichols, Gwen L., Dr. (correspondence)  
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SOURCE: Cancer Investigation, (2003) Vol. 21, No. 5, pp. 758-771.  
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ISSN: 0735-7907 CODEN: CINVD7

COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review; (Review)  
FILE SEGMENT: 016 Cancer  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index

LANGUAGE: English  
ENTRY DATE: Entered STN: 11 Dec 2003  
Last Updated on STN: 11 Dec 2003

CT Medical Descriptors:  
autocrine effect  
breast cancer: DT, drug therapy  
\*cancer therapy  
clinical trial  
colorectal cancer: DT, drug therapy  
enzyme activation  
enzyme inhibition  
gene mutation  
gene overexpression  
gene translocation  
human  
kidney carcinoma: DT, drug therapy  
lung non small cell cancer: DT, drug therapy  
lung small cell cancer: DT, drug therapy  
melanoma: DT, drug therapy  
mesothelioma: DT, drug therapy  
meta analysis  
ovary cancer: DT, drug therapy  
paracrine signaling  
phase 1 clinical trial  
phase 2 clinical trial  
phase 3 clinical trial  
priority journal  
review  
signal transduction

CT Drug Descriptors:

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology

canertinib: CT, clinical trial

canertinib: DT, drug therapy

canertinib: PD, pharmacology

carboplatin: CT, clinical trial

carboplatin: CB, drug combination

carboplatin: DT, drug therapy

cyclophosphamide: CB, drug combination

cyclophosphamide: DT, drug therapy

cytarabine: CB, drug combination

cytarabine: DT, drug therapy

doxorubicin: CT, clinical trial

doxorubicin: CB, drug combination

doxorubicin: DT, drug therapy

emd 55900

erlotinib: CT, clinical trial

erlotinib: DT, drug therapy

erlotinib: PD, pharmacology

etoposide: CB, drug combination

etoposide: DT, drug therapy

fluorouracil: CT, clinical trial

fluorouracil: CB, drug combination

fluorouracil: DT, drug therapy

gefitinib: CT, clinical trial

gefitinib: CB, drug combination

gefitinib: DT, drug therapy

gefitinib: PD, pharmacology

gemcitabine: CT, clinical trial

gemcitabine: CB, drug combination

gemcitabine: DT, drug therapy

homoharringtonine: CT, clinical trial

homoharringtonine: CB, drug combination

homoharringtonine: DT, drug therapy

humv 833: CT, clinical trial

humv 833: DT, drug therapy

humv 833: PD, pharmacology

hydroxyurea: CB, drug combination

hydroxyurea: DT, drug therapy

imatinib: CT, clinical trial

imatinib: CB, drug combination

imatinib: DT, drug therapy

imatinib: PD, pharmacology

interferon: CT, clinical trial

interferon: CB, drug combination

interferon: DT, drug therapy

irinotecan: CT, clinical trial

irinotecan: CB, drug combination

irinotecan: DT, drug therapy

oxaliplatin: CT, clinical trial

oxaliplatin: CB, drug combination

oxaliplatin: DT, drug therapy

paclitaxel: CT, clinical trial

paclitaxel: CB, drug combination

paclitaxel: DT, drug therapy

pelitinib: CT, clinical trial  
 pelitinib: DT, drug therapy  
 pelitinib: PD, pharmacology  
 phthalazine derivative: CT, clinical trial  
 phthalazine derivative: DT, drug therapy  
 phthalazine derivative: PD, pharmacology  
   \*protein tyrosine kinase inhibitor: CT, clinical trial  
   \*protein tyrosine kinase inhibitor: CB, drug combination  
   \*protein tyrosine kinase inhibitor: DT, drug therapy  
   \*protein tyrosine kinase inhibitor: PD, pharmacology  
 quinazoline derivative: CT, clinical trial  
 quinazoline derivative: DT, drug therapy  
 quinazoline derivative: PD, pharmacology  
 semaxanib: CT, clinical trial  
 semaxanib: CB, drug combination  
 semaxanib: DT, drug therapy  
 semaxanib: PD, pharmacology  
 sorafenib: CT, clinical trial  
 sorafenib: DT, drug therapy  
 sorafenib: PD, pharmacology  
 taxane derivative: CT, clinical trial  
 taxane derivative: CB, drug combination  
 taxane derivative: DT, drug therapy  
 trastuzumab: CT, clinical trial  
 trastuzumab: CB, drug combination  
 trastuzumab: DT, drug therapy  
 unclassified drug  
 unindexed drug  
 vandetanib: CT, clinical trial  
 vandetanib: DT, drug therapy  
 vandetanib: PD, pharmacology  
 RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid)  
 252916-29-3; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3;  
 (carboplatin) 41575-94-4; (cyclophosphamide) 50-18-0; (cytarabine)  
 147-94-4, 69-74-9; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib)  
 183319-69-9, 183321-74-6; (etoposide) 33419-42-0; (fluorouracil) 51-21-8;  
 (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine)  
 103882-84-4; (homoharringtonine) 26833-87-4; (hydroxyurea) 127-07-1;  
 (imatinib) 152459-95-5, 220127-57-1; (irinotecan) 100286-90-6;  
 (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (pelitinib)  
 257933-82-7; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0;  
 (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6,  
 443913-73-3  
 CN bay 43 9006; ci 1033; ekb 569; emd 55900; humv 833; iressa; osi 774; sti  
 571; su 5416; su 6668; zd 1839; zd 6474

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ACCESSION NUMBER: 2003471818 EMBASE Full-text  
 TITLE: Pharmacogenetic candidate genes for melanoma.  
 AUTHOR: Hull, Christopher; Leachman, Sancy (correspondence)  
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 SOURCE: Pharmacogenomics, (Nov 2003) Vol. 4, No. 6, pp. 753-765.  
 Refs: 140  
 ISSN: 1462-2416 CODEN: PARMFL

COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 013 Dermatology and Venereology  
 016 Cancer  
 022 Human Genetics  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 4 Dec 2003  
 Last Updated on STN: 4 Dec 2003

- AB The incidence of melanoma is rising at an alarming rate and has become an important public health concern. If detected early, melanoma carries an excellent prognosis after appropriate surgical resection. Unfortunately, advanced melanoma has a poor prognosis and is notoriously resistant to radiation and chemotherapy. The relative resistance of melanoma to a wide-range of chemotherapeutic agents and high toxicity of current therapies has prompted a search for effective alternative treatments that would improve prognosis and limit side effects. Advances in molecular genetics are revealing in increasing detail the mechanisms responsible for the development of melanoma. Hopefully, elucidation of these pathways will provide a means of screening high-risk individuals and allow new drug development for prevention and treatment by identification of specific pharmacological targets. This review will summarize the genetics of melanoma with the goal of providing insights into potential pharmacogenetic candidate genes.
- CT Medical Descriptors:  
 adverse drug reaction  
 cancer chemotherapy  
 cancer incidence  
 cancer prevention  
 cancer radiotherapy  
 cancer screening  
 cancer surgery  
 drug targeting  
 high risk patient  
 human  
 \*melanoma: DI, diagnosis  
 \*melanoma: DT, drug therapy  
 \*melanoma: ET, etiology  
 \*melanoma: PC, prevention  
 \*melanoma: SU, surgery  
 molecular genetics  
 nonhuman  
 \*pharmacogenetics  
 prognosis  
 public health  
 retrospective study  
 review  
 skin carcinogenesis
- CT Drug Descriptors:  
 5-aza-2'-deoxycytidine: DT, drug therapy  
 7-hydroxystaurosporine: DT, drug therapy  
 7-hydroxystaurosporine: PD, pharmacology  
 ARF protein: EC, endogenous compound  
 cyclin dependent kinase inhibitor: PD, pharmacology  
 flavopiridol: DT, drug therapy  
 flavopiridol: PD, pharmacology  
 helix loop helix protein: EC, endogenous compound  
 imatinib: PD, pharmacology  
 melanocortin 1 receptor: EC, endogenous compound  
 phosphatidylinositol 3,4,5 trisphosphate 3-phosphatase: EC, endogenous

compound  
 protein farnesyltransferase inhibitor: PD, pharmacology  
 protein inhibitor: PD, pharmacology  
 protein inhibitor: TP, topical drug administration  
 protein p16  
 protein p53: EC, endogenous compound  
 protein tyrosine kinase inhibitor: PD, pharmacology  
 Raf protein: EC, endogenous compound  
 Ras protein: EC, endogenous compound  
 roscovitine: DT, drug therapy  
 roscovitine: PD, pharmacology  
 sorafenib: PD, pharmacology  
 unclassified drug  
 RN (5-aza-2'-deoxycytidine) 2353-33-5; (7-hydroxystaurosporine) 112953-11-4;  
 (flavopiridol) 131740-09-5, 146426-40-6; (imatinib) 152459-95-5,  
 220127-57-1; (melanocortin 1 receptor) 234764-00-2, 234764-02-4;  
 (roscovitine) 186692-46-6; (sorafenib) 284461-73-0  
 CN (1) gleevec; bay 439006  
 CO (1) Novartis; Aventis; Cyclacel; Kyowa Hakko Kogyo

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ACCESSION NUMBER: 2003437254 EMBASE Full-text  
 TITLE: Targeting HIF-1 for cancer therapy.  
 AUTHOR: Semenza, Gregg L. (correspondence)  
 CORPORATE SOURCE: McKusick-Nathans Inst. Genetic Med., Johns Hopkins University, School of Medicine, Baltimore, MD 21287-3914, United States. gsemenza@jhmi.edu  
 SOURCE: Nature Reviews Cancer, (Oct 2003) Vol. 3, No. 10, pp. 721-732.  
 Refs: 107  
 ISSN: 1474-175X CODEN: NRCAC4  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 016 Cancer  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 13 Nov 2003  
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AB Hypoxia-inducible factor 1 (HIF-1) activates the transcription of genes that are involved in crucial aspects of cancer biology, including angiogenesis, cell survival, glucose metabolism and invasion. Intratumoral hypoxia and genetic alterations can lead to HIF-1 $\alpha$  overexpression, which has been associated with increased patient mortality in several cancer types. In preclinical studies, inhibition of HIF-1 activity has marked effects on tumour growth. Efforts are underway to identify inhibitors of HIF-1 and to test their efficacy as anticancer therapeutics.

CT Medical Descriptors:  
 angiogenesis  
 cell invasion  
 cell proliferation  
 cell survival  
 clinical trial  
 drug efficacy  
 \*drug targeting  
 enzyme activation  
 gene activity  
 gene expression

gene function  
 gene mutation  
 gene overexpression  
 \*gene targeting  
 genetic transcription  
 glucose metabolism  
 human  
 hypoxia  
 metastasis  
 nonhuman  
 oncogene  
 oncogene neu  
 priority journal  
 protein binding  
 protein degradation  
 protein modification  
 \*protein targeting  
 review  
 signal transduction  
 tissue oxygenation  
 transcription regulation  
 treatment failure  
 tumor growth

CT

Drug Descriptors:

1 benzyl 3 (5 hydroxymethyl 2 furyl)indazole: PD, pharmacology  
 1 methylpropyl 2 imidazolyl disulfide: PD, pharmacology  
 17 allylaminogeldanamycin: CT, clinical trial  
 17 allylaminogeldanamycin: PD, pharmacology  
 2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology  
 2 methoxyestradiol: CT, clinical trial  
 2 methoxyestradiol: PD, pharmacology  
 antineoplastic agent: CT, clinical trial  
 antineoplastic agent: PD, pharmacology  
 camptothecin: PD, pharmacology  
 celecoxib: CT, clinical trial  
 celecoxib: PD, pharmacology  
 erlotinib: CT, clinical trial  
 erlotinib: PD, pharmacology  
 G protein coupled receptor: EC, endogenous compound  
 gefitinib: CT, clinical trial  
 gefitinib: PD, pharmacology  
 \*hypoxia inducible factor 1: EC, endogenous compound  
 hypoxia inducible factor 1alpha: EC, endogenous compound  
 imatinib: PD, pharmacology  
 mitogen activated protein kinase: EC, endogenous compound  
 phosphatidylinositol 3 kinase: EC, endogenous compound  
 pleurotin: PD, pharmacology  
   protein tyrosine kinase inhibitor: PD, pharmacology  
 sorafenib: CT, clinical trial  
 sorafenib: PD, pharmacology  
 temsirolimus: CT, clinical trial  
 temsirolimus: PD, pharmacology  
 topotecan: PD, pharmacology  
 trastuzumab: PD, pharmacology  
 ubiquitin protein ligase: EC, endogenous compound  
 unclassified drug

RN

(1 benzyl 3 (5 hydroxymethyl 2 furyl)indazole) 170632-47-0; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (2 methoxyestradiol) 362-07-2; (camptothecin) 7689-03-4; (celecoxib) 169590-42-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6,

184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (mitogen activated protein kinase) 142243-02-5; (phosphatidylinositol 3 kinase) 115926-52-8; (sorafenib) 284461-73-0; (temsirolimus) 162635-04-3, 343261-52-9; (topotecan) 119413-54-6, 123948-87-8; (trastuzumab) 180288-69-1; (ubiquitin protein ligase) 134549-57-8  
 CN bay 439006; cci 779; glivec; herceptin; iressa; osi 774; pd 98059; yc 1; zd 1839

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ACCESSION NUMBER: 2004088284 EMBASE Full-text  
 TITLE: Targeted therapy for epithelial ovarian cancer: Current status and future prospects.  
 AUTHOR: See, H.T. (correspondence); Kavanagh, John J.; Hu, W.; Bast Jr., R.C.  
 CORPORATE SOURCE: Dept. of Gynecol. Medical Oncology, Univ. TX M. D. Anderson Cancer Ctr., Houston, TX, United States. jkavanag@mdandersono.n.org  
 AUTHOR: Kavanagh, John J.  
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 CORPORATE SOURCE: Dept. of Gynecologic Med. Oncology, MD Anderson Cancer Center, Box 401, 1515, Holcombe Boulevard, Houston, TX 77030, United States.  
 SOURCE: International Journal of Gynecological Cancer, (Nov 2003) Vol. 13, No. 6, pp. 701-734.  
 Refs: 268  
 ISSN: 1048-891X CODEN: IJGCMN  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 010 Obstetrics and Gynecology  
 016 Cancer  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 11 Mar 2004  
 Last Updated on STN: 11 Mar 2004

AB Despite advances in surgery and chemotherapy, less than 20% of patients with stage III or IV ovarian cancer survive long-term. In the past, cytotoxic regimens have been developed empirically, combining active agents at maximally tolerated doses, often without a clear rationale for their interaction. Advances in understanding the biology of ovarian cancer have identified multiple molecular targets that differ in normal and malignant cells. Targets include cell cycle regulators, growth factor receptors, signal transduction pathways, molecules that confer drug resistance, and angiogenic mechanisms. A number of targeted agents have entered clinical trials. Small molecular weight inhibitors, monoclonal antibodies, and antisense and gene therapy are all being evaluated alone and in combination with cytotoxic drugs. In contrast to earlier studies, the impact of each agent on the designated target can be assessed and agents can be matched to the genotype and phenotype of malignant and normal cells. In the long run, this should facilitate individualization of more effective, less toxic therapy for women with ovarian cancer.

CT Medical Descriptors:  
 abdominal cramp: SI, side effect  
 acne: SI, side effect



\*angiogenesis  
 animal model  
 anorexia: SI, side effect  
 \*apoptosis  
 cancer combination chemotherapy  
 cancer immunotherapy  
 cancer survival  
 cell cycle  
 cell growth  
 cell immortalization  
 cheilitis: SI, side effect  
 chemotherapy induced emesis: SI, side effect  
 clinical trial  
 dermatitis: ET, etiology  
 diarrhea: SI, side effect  
 drug approval  
 drug mechanism  
 \*drug targeting  
 enzyme activation  
 epithelium cell  
 fatigue: SI, side effect  
 female  
 \*gene therapy  
 growth regulation  
 gynecologic cancer: DR, drug resistance  
 gynecologic cancer: DT, drug therapy  
 gynecologic cancer: ET, etiology  
 human  
 human cell  
 hypertension: SI, side effect  
 interstitial lung disease: SI, side effect  
 major clinical study  
 meta analysis  
 metastasis: CO, complication  
 mouse  
 multicenter study  
 multidrug resistance  
 myalgia: SI, side effect  
 nausea: SI, side effect  
 neurotoxicity: SI, side effect  
 neutropenia: SI, side effect  
 nonhuman  
 oncogene  
 oncogene neu  
 \*ovary cancer: DR, drug resistance  
 \*ovary cancer: DT, drug therapy  
 \*ovary cancer: ET, etiology  
 phase 1 clinical trial  
 phase 2 clinical trial  
 phase 3 clinical trial  
 priority journal  
 proteinuria: SI, side effect  
 pruritus: SI, side effect  
 rash: SI, side effect  
 review  
 sensory neuropathy: SI, side effect  
 signal transduction  
 skin toxicity: ET, etiology  
 skin toxicity: SI, side effect  
 suicide gene therapy

thorax pain: SI, side effect  
 thrombocytopenia: SI, side effect  
 viral gene therapy  
 vomiting: SI, side effect  
 CT Drug Descriptors:  
 2 morpholino 8 phenylchromone: CB, drug combination  
 2 morpholino 8 phenylchromone: DT, drug therapy  
 2 morpholino 8 phenylchromone: TO, drug toxicity  
 2 morpholino 8 phenylchromone: PD, pharmacology  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AD, drug administration  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PO, oral drug administration  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology  
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: AE, adverse drug reaction  
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: CT, clinical trial  
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: AD, drug administration  
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: DT, drug therapy  
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: PO, oral drug administration  
 5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: PD, pharmacology  
 \*antineoplastic agent: AE, adverse drug reaction  
 \*antineoplastic agent: CT, clinical trial  
 \*antineoplastic agent: AD, drug administration  
 \*antineoplastic agent: CB, drug combination  
 \*antineoplastic agent: CM, drug comparison  
 \*antineoplastic agent: DO, drug dose  
 \*antineoplastic agent: IT, drug interaction  
 \*antineoplastic agent: DT, drug therapy  
 \*antineoplastic agent: TO, drug toxicity  
 \*antineoplastic agent: IP, intraperitoneal drug administration  
 \*antineoplastic agent: IV, intravenous drug administration  
 \*antineoplastic agent: PO, oral drug administration  
 \*antineoplastic agent: PK, pharmacokinetics  
 \*antineoplastic agent: PD, pharmacology  
 antisense oligonucleotide  
 atrasentan: AE, adverse drug reaction  
 atrasentan: CT, clinical trial  
 atrasentan: AD, drug administration  
 atrasentan: DT, drug therapy  
 atrasentan: IP, intraperitoneal drug administration  
 atrasentan: PD, pharmacology  
 bevacizumab: AE, adverse drug reaction  
 bevacizumab: CT, clinical trial  
 bevacizumab: AD, drug administration  
 bevacizumab: DT, drug therapy  
 bevacizumab: IV, intravenous drug administration  
 bevacizumab: PD, pharmacology

bortezomib: AE, adverse drug reaction  
 bortezomib: CT, clinical trial  
 bortezomib: CB, drug combination  
 bortezomib: DO, drug dose  
 bortezomib: DT, drug therapy  
 bortezomib: PD, pharmacology  
 \*canfosfamide: CT, clinical trial  
 \*canfosfamide: AD, drug administration  
 \*canfosfamide: CB, drug combination  
 \*canfosfamide: DO, drug dose  
 \*canfosfamide: DT, drug therapy  
 \*canfosfamide: IV, intravenous drug administration  
 \*canfosfamide: PD, pharmacology  
 cetuximab: CT, clinical trial  
 cetuximab: CB, drug combination  
 cetuximab: IT, drug interaction  
 cetuximab: DT, drug therapy  
 cetuximab: PD, pharmacology  
 cgp 69846a: CT, clinical trial  
 cgp 69846a: DT, drug therapy  
 cgp 69846a: PD, pharmacology  
 cisplatin: AE, adverse drug reaction  
 cisplatin: CT, clinical trial  
 cisplatin: CB, drug combination  
 cisplatin: CM, drug comparison  
 cisplatin: DT, drug therapy  
 epidermal growth factor receptor  
 erlotinib: AE, adverse drug reaction  
 erlotinib: CT, clinical trial  
 erlotinib: AD, drug administration  
 erlotinib: CM, drug comparison  
 erlotinib: DT, drug therapy  
 erlotinib: PO, oral drug administration  
 erlotinib: PK, pharmacokinetics  
 erlotinib: PD, pharmacology  
 gefitinib: AE, adverse drug reaction  
 gefitinib: CT, clinical trial  
 gefitinib: AD, drug administration  
 gefitinib: DT, drug therapy  
 gefitinib: PO, oral drug administration  
 gefitinib: PD, pharmacology  
 imatinib: CT, clinical trial  
 imatinib: DT, drug therapy  
 imatinib: PD, pharmacology  
 isi 3521  
 isis 3521: AE, adverse drug reaction  
 isis 3521: CT, clinical trial  
 isis 3521: DO, drug dose  
 isis 3521: DT, drug therapy  
 isis 3521: PD, pharmacology  
 \*ispinesib: CT, clinical trial  
 \*ispinesib: DT, drug therapy  
 \*ispinesib: PD, pharmacology  
 \*monoclonal antibody: AE, adverse drug reaction  
 \*monoclonal antibody: CT, clinical trial  
 \*monoclonal antibody: AD, drug administration  
 \*monoclonal antibody: CB, drug combination  
 \*monoclonal antibody: IT, drug interaction  
 \*monoclonal antibody: DT, drug therapy  
 \*monoclonal antibody: IV, intravenous drug administration

\*monoclonal antibody: PD, pharmacology  
 ONYX 015  
 peginterferon: CT, clinical trial  
 peginterferon: CB, drug combination  
 peginterferon: IT, drug interaction  
 peginterferon: DT, drug therapy  
 protein kinase C inhibitor: AE, adverse drug reaction  
 protein kinase C inhibitor: CT, clinical trial  
 protein kinase C inhibitor: DO, drug dose  
 protein kinase C inhibitor: DT, drug therapy  
 protein kinase C inhibitor: PD, pharmacology  
 protein tyrosine kinase inhibitor: CT, clinical trial  
 protein tyrosine kinase inhibitor: AD, drug administration  
 protein tyrosine kinase inhibitor: DT, drug therapy  
 protein tyrosine kinase inhibitor: PO, oral drug administration  
 protein tyrosine kinase inhibitor: PK, pharmacokinetics  
 protein tyrosine kinase inhibitor: PD, pharmacology

\*sorafenib: AE, adverse drug reaction  
 \*sorafenib: CT, clinical trial  
 \*sorafenib: AD, drug administration  
 \*sorafenib: DT, drug therapy  
 \*sorafenib: PO, oral drug administration  
 \*sorafenib: PK, pharmacokinetics  
 \*sorafenib: PD, pharmacology  
 tamoxifen: CT, clinical trial  
 tamoxifen: CM, drug comparison  
 tamoxifen: DT, drug therapy  
 tanomastat: CT, clinical trial  
 tanomastat: DT, drug therapy  
 tanomastat: PD, pharmacology  
 thalidomide: CT, clinical trial  
 thalidomide: CM, drug comparison  
 thalidomide: DT, drug therapy  
 tipifarnib: AE, adverse drug reaction  
 tipifarnib: CT, clinical trial  
 tipifarnib: AD, drug administration  
 tipifarnib: DT, drug therapy  
 tipifarnib: PO, oral drug administration  
 tipifarnib: PD, pharmacology  
 trastuzumab: CT, clinical trial  
 trastuzumab: CB, drug combination  
 trastuzumab: IT, drug interaction  
 trastuzumab: DT, drug therapy  
 trastuzumab: PD, pharmacology  
 unclassified drug  
 unindexed drug  
 vatalanib: AD, drug administration  
 vatalanib: DT, drug therapy  
 vatalanib: PO, oral drug administration  
 vatalanib: PK, pharmacokinetics  
 vatalanib: PD, pharmacology  
 virus vector

RN (2 morpholino 8 phenylchromone) 154447-36-6; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide) 99519-84-3; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (bevacizumab) 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5; (canfosfamide) 158382-37-7, 439943-59-6; (cetuximab) 205923-56-4; (cgp 69846a) 177075-18-2; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2,

184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (isis 3521) 151879-73-1; (ispinesib) 336113-53-2, 514820-03-2; (sorafenib) 284461-73-0; (tamoxifen) 10540-29-1; (tanomastat) 179545-76-7, 179545-77-8; (thalidomide) 50-35-1; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1; (vatalanib) 212141-54-3, 212142-18-2

CN (1) avastin; (2) erbitux; (3) gleevec; (4) herceptin; (5) imc c225; (6) iressa; (7) ONYX 015; (8) osi 774; (9) ps 341; (10) r 115777; (11) sti 571; (12) tarceva; (13) tlk 286; (14) velcade; (15) zarnestra; (16) zd 1839; bay 12 9566; bay 43 9006; isi 3521; isis 5132; ly 294002; pkc 787; sb 715992; su 6668

CO (1) Genentech (United States); (2) Imclone (United States); (3) Novartis (Switzerland); (4) Genentech (United States); (5) Imclone (United States); (6) Astra Zeneca (United Kingdom); (7) Onyx (United States); (8) Osi (United States); (9) Millennium Pharmaceuticals (United States); (10) Johnson and Johnson (United States); (11) Novartis (Switzerland); (12) Osi (United States); (13) Telik (United States); (14) Millennium Pharmaceuticals (United States); (15) Johnson and Johnson (United States); (16) Astra Zeneca (United Kingdom)

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ACCESSION NUMBER: 2003481481 EMBASE Full-text

TITLE: The impact of anti-angiogenic agents on cancer therapy.

AUTHOR: Marme, Dieter (correspondence)

CORPORATE SOURCE: Tumor Biology Center, Institute of Molecular Oncology, Breisacherstrasse 117, 79106 Freiburg, Germany. marme@tumor.bio.uni-freiburg.de

SOURCE: Journal of Cancer Research and Clinical Oncology, (Nov 2003) Vol. 129, No. 11, pp. 607-620.  
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FILE SEGMENT: 016 Cancer  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Dec 2003  
Last Updated on STN: 29 Dec 2003

CT Medical Descriptors:  
angiogenesis  
breast cancer: DT, drug therapy  
\*cancer: DT, drug therapy  
\*cancer chemotherapy  
cancer combination chemotherapy  
cancer inhibition  
cancer model  
cell transformation  
clinical trial  
colorectal cancer: DT, drug therapy  
drug effect  
drug efficacy  
drug mechanism  
drug potency  
drug safety  
drug targeting  
drug tolerability  
endothelium cell  
glioblastoma: DT, drug therapy

human  
 IC 50  
 kidney carcinoma: DT, drug therapy  
 leukemia: DT, drug therapy  
 liver metastasis: CO, complication  
 liver metastasis: DT, drug therapy  
 lung hemorrhage: SI, side effect  
 lung non small cell cancer: DT, drug therapy  
 melanoma: DT, drug therapy  
 nonhodgkin lymphoma: DT, drug therapy

nonhuman  
 oncogene  
 pancreas cancer: DT, drug therapy  
 priority journal  
 protein family  
 radioimmunotherapy  
 regulatory mechanism  
 review  
 side effect: SI, side effect  
 signal transduction  
 stem cell  
 tumor growth  
 tumor suppressor gene  
 tumor vascularization

CT

Drug Descriptors:  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy  
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology  
 4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: CT, clinical trial  
 4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: DT, drug therapy  
 4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: PD, pharmacology  
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one  
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: CT, clinical trial  
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: DT, drug therapy  
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: PO, oral drug administration  
 5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: PD, pharmacology  
 a 422885 66  
 aal 993  
 ag 13925  
 alpha2b interferon: CB, drug combination  
 alpha2b interferon: DT, drug therapy  
 alpha2b interferon: PD, pharmacology  
 \*angiogenesis inhibitor: AE, adverse drug reaction

\*angiogenesis inhibitor: CT, clinical trial  
 \*angiogenesis inhibitor: CB, drug combination  
 \*angiogenesis inhibitor: CM, drug comparison  
 \*angiogenesis inhibitor: DO, drug dose  
 \*angiogenesis inhibitor: DT, drug therapy  
 \*angiogenesis inhibitor: PO, oral drug administration  
 \*angiogenesis inhibitor: PK, pharmacokinetics  
 \*angiogenesis inhibitor: PD, pharmacology  
 angiozyme: CT, clinical trial  
 angiozyme: CB, drug combination  
 angiozyme: DT, drug therapy  
 angiozyme: PD, pharmacology  
 antineoplastic agent: AE, adverse drug reaction  
 antineoplastic agent: CT, clinical trial  
 antineoplastic agent: CB, drug combination  
 antineoplastic agent: CM, drug comparison  
 antineoplastic agent: DO, drug dose  
 antineoplastic agent: DT, drug therapy  
 antineoplastic agent: PO, oral drug administration  
 antineoplastic agent: PD, pharmacology  
 axitinib: CT, clinical trial  
 axitinib: CB, drug combination  
 axitinib: DT, drug therapy  
 axitinib: PD, pharmacology  
 bevacizumab: AE, adverse drug reaction  
 bevacizumab: CT, clinical trial  
 bevacizumab: CB, drug combination  
 bevacizumab: DT, drug therapy  
 bevacizumab: PD, pharmacology  
 bsf 466895  
 carbazole derivative: CT, clinical trial  
 carbazole derivative: DT, drug therapy  
 carbazole derivative: PO, oral drug administration  
 carbazole derivative: PD, pharmacology  
 cetuximab  
 chlr 258  
 cilengitide: AE, adverse drug reaction  
 cilengitide: CT, clinical trial  
 cilengitide: DO, drug dose  
 cilengitide: DT, drug therapy  
 cilengitide: PK, pharmacokinetics  
 cilengitide: PD, pharmacology  
 cnt 095  
 cp 547 632: AE, adverse drug reaction  
 cp 547 632: CT, clinical trial  
 cp 547 632: DT, drug therapy  
 cp 547 632: PD, pharmacology  
 docetaxel: CB, drug combination  
 docetaxel: DT, drug therapy  
 docetaxel: PD, pharmacology  
 e 7080  
 emd 7200  
 erlotinib  
 gefitinib: DT, drug therapy  
 gefitinib: PD, pharmacology  
 gw 2286  
 gw 654652  
 imatinib  
 imc 1c11  
 isis 3521

isothiazole derivative: AE, adverse drug reaction  
 isothiazole derivative: CT, clinical trial  
 isothiazole derivative: DT, drug therapy  
 isothiazole derivative: PD, pharmacology  
 krn 633  
 l 19  
 ll 4  
 midostaurin  
 monoclonal antibody DC101: CT, clinical trial  
 monoclonal antibody DC101: DT, drug therapy  
 monoclonal antibody DC101: PD, pharmacology  
 monoclonal antibody IMC 1C11: CT, clinical trial  
 monoclonal antibody IMC 1C11: DT, drug therapy  
 monoclonal antibody IMC 1C11: PD, pharmacology  
 monoclonal antibody lm 609: CT, clinical trial  
 monoclonal antibody lm 609: DT, drug therapy  
 monoclonal antibody lm 609: PD, pharmacology  
 n acetylcholinol phosphate  
 pd 166285  
 PD 173074  
   protein tyrosine kinase inhibitor: AE, adverse drug reaction  
   protein tyrosine kinase inhibitor: CT, clinical trial  
   protein tyrosine kinase inhibitor: CE, drug combination  
   protein tyrosine kinase inhibitor: CM, drug comparison  
   protein tyrosine kinase inhibitor: DO, drug dose  
   protein tyrosine kinase inhibitor: DT, drug therapy  
   protein tyrosine kinase inhibitor: PO, oral drug administration  
   protein tyrosine kinase inhibitor: PD, pharmacology  
 receptor antibody: CT, clinical trial  
 receptor antibody: DT, drug therapy  
 receptor antibody: PD, pharmacology  
 rwj 417975  
 sorafenib  
 su 11657  
 sunitinib: CT, clinical trial  
 sunitinib: DT, drug therapy  
 sunitinib: PD, pharmacology  
 temozolomide: CM, drug comparison  
 temozolomide: DT, drug therapy  
 temozolomide: PD, pharmacology  
 trastuzumab: DT, drug therapy  
 trastuzumab: PD, pharmacology  
 unclassified drug  
 unindexed drug  
 vandetanib: CT, clinical trial  
 vandetanib: DT, drug therapy  
 vandetanib: PD, pharmacology  
 vasculotropin antibody: CM, drug comparison  
 vasculotropin antibody: DT, drug therapy  
 vasculotropin antibody: PD, pharmacology  
 vasculotropin receptor 2 antibody: CT, clinical trial  
 vasculotropin receptor 2 antibody: DT, drug therapy  
 vasculotropin receptor 2 antibody: PD, pharmacology  
 vasculotropin receptor 2 inhibitor: AE, adverse drug reaction  
 vasculotropin receptor 2 inhibitor: CT, clinical trial  
 vasculotropin receptor 2 inhibitor: DT, drug therapy  
 vasculotropin receptor 2 inhibitor: PO, oral drug administration  
 vasculotropin receptor 2 inhibitor: PD, pharmacology  
 vasculotropin trap: CT, clinical trial  
 vasculotropin trap: CM, drug comparison



vasculotropin trap: DT, drug therapy  
 vasculotropin trap: PK, pharmacokinetics  
 vasculotropin trap: PD, pharmacology  
 vatalanib: CT, clinical trial  
 vatalanib: CB, drug combination  
 vatalanib: DO, drug dose  
 vatalanib: DT, drug therapy  
 vatalanib: PD, pharmacology  
 zk 260 255

- RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid)  
 252916-29-3; (alpha2b interferon) 99210-65-8; (axitinib) 319460-85-0;  
 (bevacizumab) 216974-75-3; (cetuximab) 205923-56-4; (cilengitide)  
 188968-51-6; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9,  
 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gw 2286)  
 601517-74-2; (imatinib) 152459-95-5, 220127-57-1; (isis 3521) 151879-73-1;  
 (midostaurin) 120685-11-2; (n acetylcolchinal phosphate) 219923-05-4;  
 (sorafenib) 284461-73-0; (sunitinib) 341031-54-7, 557795-19-4;  
 (temozolomide) 85622-93-1; (trastuzumab) 180288-69-1; (vandetanib)  
 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib) 212141-54-3,  
 212142-18-2
- CN (1) a 422885 66; (2) aal 993; (3) ag 013736; (4) ag 13925; (5) azd 2171;  
 (6) azd 6474; (7) bay 43 9006; (8) bsf 466895; (9) cep 7055; (10) cep  
 7055; (11) chir 258; (12) cnt 950; (13) cp 547 632; (14) e 7080; (15) emd  
 121974; (16) emd 7200; (17) emd 7200; (18) gleevec; (19) gw 2286; (20) gw  
 654652; (21) herceptin; (22) imc 1c11; (23) imc c225; (24) iressa; (25)  
 isis 3521; (26) isis 3521; (27) krn 633; (28) l 19; (29) ll 4; (30) pd  
 166285; (31) PD 173074; (32) pkc 412; (33) ptk 787; (34) ptk 787; (35) rwj  
 417975; (36) su 11248; (37) su 11657; (38) su 6668; (39) tarceva; (40)  
 tarceva; (41) tarceva; (42) tsu 68; (43) vitaxin; (44) zd 6126; (45) zk  
 222584; (46) zk 222584; (47) zk 260 255; cep 5214
- CO (1) Abbott (United States); (2) Novartis; (3) Pfizer (United States); (4)  
 Agouron (United States); (5) Astra Zeneca (United Kingdom); (6) Astra  
 Zeneca (United Kingdom); (7) Bayer (United States); (8) Abbott (United  
 States); (9) Cephalon (United States); (10) Sanofi Synthelabo (France);  
 (11) Chiron (United States); (12) Centocor (United States); (13) Pfizer  
 (United States); (14) Eisai (Japan); (15) Merck (Denmark); (16) Bms  
 (United States); (17) Merck (Denmark); (18) Novartis; (19) Glaxo Wellcome  
 (United States); (20) Glaxo SmithKline (United States); (21) Genentech;  
 (22) Glaxo SmithKline (United States); (23) Imclone (United States); (24)  
 Astra Zeneca (United Kingdom); (25) Isis (United States); (26) Novartis;  
 (27) Kirin (Japan); (28) university of zurich; (29) University College  
 London (United Kingdom); (30) Pfizer (United States); (31) Pfizer (United  
 States); (32) Novartis; (33) Novartis (Germany); (34) Schering (Germany);  
 (35) RW Johnson (United States); (36) Sugen (United States); (37) Sugen  
 (United States); (38) Sugen (United States); (39) Genentech (United  
 States); (40) Hoffmann La Roche; (41) Osi (United States); (42) Taiko  
 (Japan); (43) Medimmune (United States); (44) Astra Zeneca (United  
 Kingdom); (45) Novartis (Germany); (46) Schering (Germany); (47) Novartis;  
 albert einstein (United States); Bristol Myers Squibb (United States);  
 indiana university (United States); Oxigene (United States); peregrine  
 (United States); Regeneron (United States); Ribozyne Pharmaceuticals  
 (United States); scribbs clinic (United States)

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ACCESSION NUMBER: 2003500287 EMBASE [Full-text](#)

TITLE: Highlights of the 39th Annual Meeting of the American  
 Society of Clinical Oncology.

AUTHOR: Prescott, Lawrence M.

SOURCE: P and T, (Aug 2003) Vol. 28, No. 8, pp. 528-531.

ISSN: 1052-1372 CODEN: PPTTEK  
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 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)  
 FILE SEGMENT: 016 Cancer  
 026 Immunology, Serology and Transplantation  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
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 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 29 Dec 2003  
 Last Updated on STN: 29 Dec 2003

- AB More than 25,000 oncologists, research scientists, cancer nurses, and other health care professionals from around the world gathered at the 39th Annual Meeting of the American Society of Clinical Oncology, held in Chicago, Illinois, from May 31 to June 3, 2003, to hear the latest developments in the epidemiology, prevention, diagnosis, and treatment of a variety of cancers. The most recent studies included novel therapeutic combinations and new chemotherapeutic and biological agents for the treatment of metastatic breast cancer, bronchoalveolar cell carcinoma, pancreatic cancer, colorectal cancer, melanoma, and hematologic malignancies as well as advances in the management of chemotherapy-induced adverse effects.
- CT Medical Descriptors:  
 advanced cancer: DT, drug therapy  
 \*anemia: DT, drug therapy  
 \*anemia: SI, side effect  
 bone marrow toxicity: SI, side effect  
 breast cancer: DT, drug therapy  
 \*cancer: DT, drug therapy  
 \*cancer chemotherapy  
 cancer combination chemotherapy  
 \*cancer immunotherapy  
 cancer survival  
 chemotherapy induced emesis: SI, side effect  
 chronic lymphatic leukemia: DT, drug therapy  
 clinical trial  
 colorectal cancer: DT, drug therapy  
 conference paper  
 diarrhea: SI, side effect  
 drug efficacy  
 drug safety  
 febrile neutropenia: SI, side effect  
 fever: SI, side effect  
 human  
 lung alveolus cell carcinoma: DT, drug therapy  
 lymphadenopathy: SI, side effect  
 major clinical study  
 melanoma: DT, drug therapy  
 metastasis: CO, complication  
 metastasis: DT, drug therapy  
 multicenter study  
 nausea: SI, side effect  
 neuropathy: SI, side effect  
 neutropenia: SI, side effect  
 nonhodgkin lymphoma: DT, drug therapy  
 pancreas cancer: DT, drug therapy  
 phase 1 clinical trial  
 phase 2 clinical trial  
 side effect: SI, side effect  
 skin toxicity: SI, side effect

treatment outcome  
vomiting: SI, side effect

CT Drug Descriptors:

- \*antineoplastic agent: AE, adverse drug reaction
- \*antineoplastic agent: CT, clinical trial
- \*antineoplastic agent: AD, drug administration
- \*antineoplastic agent: CB, drug combination
- \*antineoplastic agent: CM, drug comparison
- \*antineoplastic agent: DO, drug dose
- \*antineoplastic agent: DT, drug therapy
- \*antineoplastic agent: IV, intravenous drug administration
- \*antineoplastic agent: PO, oral drug administration
- \*cancer vaccine: AE, adverse drug reaction
- \*cancer vaccine: CT, clinical trial
- \*cancer vaccine: AD, drug administration
- \*cancer vaccine: DT, drug therapy
- \*cancer vaccine: DL, intradermal drug administration
- \*cancer vaccine: PR, pharmaceuticals
- \*cancer vaccine: SC, subcutaneous drug administration
- carboplatin: AE, adverse drug reaction
- carboplatin: CT, clinical trial
- carboplatin: CB, drug combination
- carboplatin: DO, drug dose
- carboplatin: DT, drug therapy
- carcinoembryonic antigen
- cetuximab: CT, clinical trial
- cetuximab: CB, drug combination
- cetuximab: CM, drug comparison
- cetuximab: DT, drug therapy
- cyclophosphamide: AE, adverse drug reaction
- cyclophosphamide: CT, clinical trial
- cyclophosphamide: CB, drug combination
- cyclophosphamide: DT, drug therapy
- docetaxel: AE, adverse drug reaction
- docetaxel: CT, clinical trial
- docetaxel: CB, drug combination
- docetaxel: DT, drug therapy
- doxorubicin: AE, adverse drug reaction
- doxorubicin: CT, clinical trial
- doxorubicin: CB, drug combination
- doxorubicin: DT, drug therapy
- \*erlotinib: CT, clinical trial
- \*erlotinib: DT, drug therapy
- fludarabine: CT, clinical trial
- fludarabine: CB, drug combination
- fludarabine: DT, drug therapy
- fludarabine phosphate
- fluorouracil: AE, adverse drug reaction
- fluorouracil: CT, clinical trial
- fluorouracil: CB, drug combination
- fluorouracil: DO, drug dose
- fluorouracil: DT, drug therapy
- fluorouracil: IV, intravenous drug administration
- folfinirinox: AE, adverse drug reaction
- folfinirinox: CT, clinical trial
- folfinirinox: DO, drug dose
- folfinirinox: DT, drug therapy
- folfinirinox: IV, intravenous drug administration
- granulocyte macrophage colony stimulating factor
- irinotecan: AE, adverse drug reaction

irinotecan: CT, clinical trial  
 irinotecan: CB, drug combination  
 irinotecan: CM, drug comparison  
 irinotecan: DO, drug dose  
 irinotecan: DT, drug therapy  
 irinotecan: IV, intravenous drug administration  
 \*monoclonal antibody: AE, adverse drug reaction  
 \*monoclonal antibody: CT, clinical trial  
 \*monoclonal antibody: CB, drug combination  
 \*monoclonal antibody: CM, drug comparison  
 \*monoclonal antibody: DT, drug therapy  
 nevsar  
 novel erythropoiesis stimulating protein: CT, clinical trial  
 novel erythropoiesis stimulating protein: CM, drug comparison  
 novel erythropoiesis stimulating protein: DO, drug dose  
 novel erythropoiesis stimulating protein: DT, drug therapy  
 oblimersen: AE, adverse drug reaction  
 oblimersen: CT, clinical trial  
 oblimersen: CB, drug combination  
 oblimersen: DT, drug therapy  
 oblimersen: PD, pharmacology  
 oxaliplatin: AE, adverse drug reaction  
 oxaliplatin: CT, clinical trial  
 oxaliplatin: CB, drug combination  
 oxaliplatin: DO, drug dose  
 oxaliplatin: DT, drug therapy  
 oxaliplatin: IV, intravenous drug administration  
 paclitaxel: AE, adverse drug reaction  
 paclitaxel: CT, clinical trial  
 paclitaxel: CB, drug combination  
 paclitaxel: DO, drug dose  
 paclitaxel: DT, drug therapy  
 prednisone: AE, adverse drug reaction  
 prednisone: CT, clinical trial  
 prednisone: CB, drug combination  
 prednisone: DT, drug therapy  
 protein bcl 2  
 protein kinase inhibitor: AE, adverse drug reaction  
 protein kinase inhibitor: CT, clinical trial  
 protein kinase inhibitor: AD, drug administration  
 protein kinase inhibitor: CB, drug combination  
 protein kinase inhibitor: DO, drug dose  
 protein kinase inhibitor: DT, drug therapy  
 protein kinase inhibitor: PO, oral drug administration  
 protein kinase inhibitor: PD, pharmacology  
   protein tyrosine kinase inhibitor: CT, clinical trial  
   protein tyrosine kinase inhibitor: DT, drug therapy  
 Raf protein  
 recombinant erythropoietin: CT, clinical trial  
 recombinant erythropoietin: CM, drug comparison  
 recombinant erythropoietin: DT, drug therapy  
 rituximab: AE, adverse drug reaction  
 rituximab: CT, clinical trial  
 rituximab: CB, drug combination  
 rituximab: DT, drug therapy  
 \*sorafenib: AE, adverse drug reaction  
 \*sorafenib: CT, clinical trial  
 \*sorafenib: AD, drug administration  
 \*sorafenib: CB, drug combination  
 \*sorafenib: DO, drug dose

\*sorafenib: DT, drug therapy  
 \*sorafenib: PO, oral drug administration  
 \*sorafenib: PD, pharmacology  
 trastuzumab: AE, adverse drug reaction  
 trastuzumab: CT, clinical trial  
 trastuzumab: CB, drug combination  
 trastuzumab: DT, drug therapy  
 TRICOM vaccine  
 unclassified drug  
 unindexed drug  
 vincristine: AE, adverse drug reaction  
 vincristine: CT, clinical trial  
 vincristine: CB, drug combination  
 vincristine: DT, drug therapy

RN (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (cyclophosphamide) 50-18-0; (docetaxel) 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (fludarabine phosphate) 75607-67-9; (fludarabine) 21679-14-1; (fluorouracil) 51-21-8; (irinotecan) 100286-90-6; (oblimersen) 190977-41-4; (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (prednisone) 53-03-2; (protein bcl 2) 219306-68-0; (recombinant erythropoietin) 113427-24-0, 122312-54-3, 130455-76-4; (rituximab) 174722-31-7; (sorafenib) 384461-73-0; (trastuzumab) 180288-69-1; (vincristine) 57-22-7

CN (1) aranesp; (2) bay 43 9006; (3) camptosar; (4) eloxatin; (5) erbitux; (6) erbitux; (7) fludara; (8) genasense; (9) herceptin; (10) paraplalin; (11) procrit; (12) rituxan; (13) rituxan; (14) tarceva; (15) taxol; (16) taxotere; (17) TRICOM vaccine; cytoxan; endoxan; nevsar

CO (1) Amgen; (2) Bayer; (3) Pharmacia; (4) Sanofi Synthelabo; (5) Imclone; (6) Merck; (7) Berlex; (8) Genta; (9) Genentech; (10) Bristol Myers Squibb; (11) Ortho; (12) Genentech; (13) Idec; (14) Genentech; (15) Bristol Myers Squibb; (16) Aventis; (17) Therion

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ACCESSION NUMBER: 2003156049 EMBASE Full-text  
 TITLE: Signal transduction modulators for cancer therapy: From promise to practice?  
 AUTHOR: Lobbezoo, Marinus W., Dr. (correspondence); Van Kalken, Coenraad  
 CORPORATE SOURCE: NDDO Research Foundation, Amsterdam, Netherlands. lobbezoo@euronet.nl  
 AUTHOR: Giaccone, Giuseppe  
 CORPORATE SOURCE: VU Medical Center, Amsterdam, Netherlands.  
 SOURCE: Oncologist, (2003) Vol. 8, No. 2, pp. 210-213.  
 Refs: 3  
 ISSN: 1083-7159 CODEN: OCOLF6  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)  
 FILE SEGMENT: 016 Cancer  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 9 May 2003  
 Last Updated on STN: 9 May 2003

CT Medical Descriptors:  
 cancer: DT, drug therapy  
 \*cancer chemotherapy  
 clinical trial  
 conference paper

drug approval  
 drug design  
 drug screening  
 drug targeting  
 food and drug administration  
 human  
 priority journal  
 side effect: SI, side effect  
 \*signal transduction  
 CT Drug Descriptors:  
 1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene  
 17 allylamino 17 demethoxygeldanamycin: DV, drug development  
 2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: DV,  
 drug development  
 4 [6 methoxy 7 [3 (1 piperidinyl)propoxy] 4 quinazolinyl] 1  
 piperazinecarboxylic acid (4 isopropoxyphenyl)amide: DV, drug development  
 6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3  
 d]pyrimidine  
 7 hydroxystaurosporine  
 \*antineoplastic agent: AE, adverse drug reaction  
 \*antineoplastic agent: CT, clinical trial  
 \*antineoplastic agent: CB, drug combination  
 \*antineoplastic agent: DV, drug development  
 \*antineoplastic agent: DT, drug therapy  
 \*antineoplastic agent: PO, oral drug administration  
 \*antineoplastic agent: PD, pharmacology  
 ap23451: DV, drug development  
 bevacizumab: CT, clinical trial  
 bevacizumab: CB, drug combination  
 bevacizumab: DV, drug development  
 bevacizumab: DT, drug therapy  
 bevacizumab: PD, pharmacology  
 bortezomib  
 canertinib: DV, drug development  
 cetuximab: DV, drug development  
 cpd 5: DV, drug development  
 ct 32228: DV, drug development  
 erlotinib: AE, adverse drug reaction  
 erlotinib: CT, clinical trial  
 erlotinib: DV, drug development  
 erlotinib: DT, drug therapy  
 erlotinib: PD, pharmacology  
 flavopiridol: DV, drug development  
 gefitinib: AE, adverse drug reaction  
 gefitinib: CT, clinical trial  
 gefitinib: DV, drug development  
 gefitinib: DT, drug therapy  
 gefitinib: PD, pharmacology  
 gw 211: DV, drug development  
 imatinib: DV, drug development  
 imc 1c11: DV, drug development  
 imc 2c6: DV, drug development  
 imc 1c11  
 matuzumab: DV, drug development  
 n acetylcolchicol phosphate  
 pertuzumab: DV, drug development  
   protein tyrosine kinase  
 semaxanib: DV, drug development  
 signal transduction modulator: AE, adverse drug reaction  
 signal transduction modulator: CT, clinical trial

signal transduction modulator: CB, drug combination  
 signal transduction modulator: DV, drug development  
 signal transduction modulator: DT, drug therapy  
 signal transduction modulator: PO, oral drug administration  
 signal transduction modulator: PD, pharmacology  
 sorafenib: DV, drug development  
 sunitinib: CT, clinical trial  
 sunitinib: DV, drug development  
 sunitinib: DT, drug therapy  
 sunitinib: PO, oral drug administration  
 sunitinib: PD, pharmacology  
 temsirolimus: DV, drug development  
 tipifarnib: DV, drug development  
 trastuzumab: DV, drug development  
 unclassified drug  
 unindexed drug  
 vandetanib  
 RN (1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene) 109511-58-2;  
 (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide)  
 212631-79-3; (7 hydroxystaurosporine) 112953-11-4; (bevacizumab)  
 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5; (canertinib)  
 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4;  
 (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5,  
 146426-40-6; (gefitinib) 184475-35-2, 184475-56-6, 184475-56-7; (imatinib)  
 152459-95-5, 220127-57-1; (matuzumab) 339186-68-4; (n acetylcolchinal  
 phosphate) 219923-05-4; (protein tyrosine kinase)  
 80449-02-1; (semaxanib) 186610-95-7; (sorafenib) 234461-73-0;  
 (sunitinib) 341031-54-7, 557795-19-4; (temsirolimus) 162635-04-3,  
 343261-52-9; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1;  
 (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3  
 CN ap23451; bay 43 9006; c225; cci 779; ci 1033; ci 1040; cpd 5; ct 32228; ct  
 53518; emd 72000; gw 211; imc 2c6; imc ic11; osi 774; pki 166; ps 341;  
 r115777; st1571; su11248; su5416; u0126; ucn 01; zd1839; zd6126; zd6474

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ACCESSION NUMBER: 2003436243 EMBASE Full-text  
 TITLE: The pipeline of new anticancer agents for breast cancer  
 treatment in 2003.  
 AUTHOR: Awada, A. (correspondence); Cardoso, F.; Atalay, G.;  
 Giuliani, R.; Mano, M.; Piccart, M.J.  
 CORPORATE SOURCE: Jules Bordet Institute, Chemotherapy Unit, Boulevard de  
 Waterloo 125, 1000 Brussels, Belgium. ahmad.awada@bordet.be  
 SOURCE: Critical Reviews in Oncology/Hematology, (Oct 2003) Vol.  
 48, No. 1, pp. 45-63.  
 Refs: 172  
 ISSN: 1040-8428 CODEN: CCRHEC  
 COUNTRY: Ireland  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 016 Cancer  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 13 Nov 2003  
 Last Updated on STN: 13 Nov 2003

AB In recent years, strategy in cancer therapy in general, and breast cancer in  
 particular, has been the use of maximum tolerated doses of toxic non-specific  
 agents as well as the investigation of a range of new agents that specifically

target tumor-related molecules, in a variety of biological pathways. The trial of chemotherapy (CT) versus chemotherapy+trastuzumab (Herceptin®) in HER-2-overexpressing metastatic breast cancer (MBC) was one of the first to use a biological agent in combination with chemotherapy with success and, together with some trials of taxanes in anthracycline-resistance patients one of the few to demonstrate an overall survival (OS) advantage in MBC. Five main molecular pathways are of particular interest in terms of new drug development in breast cancer: the estrogen receptor (ER) pathway, the tyrosine kinase signal transduction pathway, the cell cycle regulation pathway, the apoptosis pathway and the angiogenesis pathway. This review will focus on new agents, cytotoxic, hormonal and molecular-targeted, which are in advanced clinical stages of development for the treatment of MBC. .COPYRGHT. 2003 Elsevier Ireland Ltd. All rights reserved.

CT Medical Descriptors:  
alopecia: SI, side effect  
anemia: SI, side effect  
angiogenesis  
anorexia: SI, side effect  
antineoplastic activity  
apoptosis  
arthralgia: SI, side effect  
asthenia: SI, side effect  
blood toxicity: SI, side effect  
\*breast cancer: DR, drug resistance  
\*breast cancer: DT, drug therapy  
cancer chemotherapy  
cancer survival  
cardiotoxicity: SI, side effect  
cell cycle  
chemotherapy induced emesis: SI, side effect  
clinical trial  
congestive heart failure: SI, side effect  
constipation: SI, side effect  
diarrhea: SI, side effect  
drug effect  
drug efficacy  
drug eruption: SI, side effect  
drug targeting  
fatigue: SI, side effect  
febrile neutropenia: SI, side effect  
gastrointestinal symptom: SI, side effect  
gene therapy  
hand foot syndrome: SI, side effect  
human  
leukopenia: SI, side effect  
metastasis: DT, drug therapy  
mucosa inflammation: SI, side effect  
myalgia: SI, side effect  
nausea: SI, side effect  
neuropathy: SI, side effect  
neurotoxicity: SI, side effect  
neutropenia: SI, side effect  
peripheral neuropathy: SI, side effect  
review  
sensory neuropathy: SI, side effect  
side effect: SI, side effect  
signal transduction  
stomatitis: SI, side effect  
thrombocytopenia: SI, side effect  
transaminitis: SI, side effect



CT Drug Descriptors:  
 3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide  
 angiogenesis inhibitor: DT, drug therapy  
 angiogenesis inhibitor: PD, pharmacology  
 anthracycline derivative: AE, adverse drug reaction  
 anthracycline derivative: CT, clinical trial  
 anthracycline derivative: CB, drug combination  
 anthracycline derivative: CM, drug comparison  
 anthracycline derivative: DT, drug therapy  
 anthracycline derivative: PD, pharmacology  
 antimetabolite: AE, adverse drug reaction  
 antimetabolite: CB, drug combination  
 antimetabolite: DT, drug therapy  
 antimetabolite: PO, oral drug administration  
 antimetabolite: PD, pharmacology  
 \*antineoplastic agent: AE, adverse drug reaction  
 \*antineoplastic agent: CT, clinical trial  
 \*antineoplastic agent: CB, drug combination  
 \*antineoplastic agent: CM, drug comparison  
 \*antineoplastic agent: DT, drug therapy  
 \*antineoplastic agent: IP, intraperitoneal drug administration  
 \*antineoplastic agent: TU, intratumoral drug administration  
 \*antineoplastic agent: PO, oral drug administration  
 \*antineoplastic agent: PD, pharmacology  
 aromatase inhibitor: DT, drug therapy  
 aromatase inhibitor: PD, pharmacology  
 arzoxifene: DT, drug therapy  
 arzoxifene: PD, pharmacology  
 bms 184476: CT, clinical trial  
 bms 184476: CM, drug comparison  
 bms 184476: DT, drug therapy  
 bms 184476: PD, pharmacology  
 bortezomib  
 canertinib  
 cc 7085  
 cdc 801  
 cgp 69846a  
 cm 101  
 cyclooxygenase 2 inhibitor: CT, clinical trial  
 cyclooxygenase 2 inhibitor: DT, drug therapy  
 cyclooxygenase 2 inhibitor: PD, pharmacology  
 cytotoxic agent: AE, adverse drug reaction  
 cytotoxic agent: CT, clinical trial  
 cytotoxic agent: CB, drug combination  
 cytotoxic agent: CM, drug comparison  
 cytotoxic agent: DT, drug therapy  
 cytotoxic agent: IP, intraperitoneal drug administration  
 cytotoxic agent: TU, intratumoral drug administration  
 cytotoxic agent: PO, oral drug administration  
 cytotoxic agent: PD, pharmacology  
 DNA topoisomerase inhibitor: AE, adverse drug reaction  
 DNA topoisomerase inhibitor: CT, clinical trial  
 DNA topoisomerase inhibitor: DT, drug therapy  
 DNA topoisomerase inhibitor: PD, pharmacology  
 docetaxel: AE, adverse drug reaction  
 docetaxel: CT, clinical trial  
 docetaxel: CM, drug comparison  
 docetaxel: DT, drug therapy  
 docetaxel: PD, pharmacology  
 doxorubicin

erlotinib  
 fulvestrant: CT, clinical trial  
 fulvestrant: DT, drug therapy  
 fulvestrant: PD, pharmacology  
 gefitinib: CT, clinical trial  
 gefitinib: DT, drug therapy  
 gefitinib: PD, pharmacology  
 ixabepilone: AE, adverse drug reaction  
 ixabepilone: CT, clinical trial  
 ixabepilone: DT, drug therapy  
 ixabepilone: PD, pharmacology  
 lapatinib  
 lenalidomide  
 letrozole: CT, clinical trial  
 letrozole: CM, drug comparison  
 letrozole: DT, drug therapy  
 letrozole: PD, pharmacology  
 lonafarnib  
 marimastat  
 navelbine: CT, clinical trial  
 navelbine: DT, drug therapy  
 navelbine: PO, oral drug administration  
 navelbine: PD, pharmacology  
 paclitaxel: AE, adverse drug reaction  
 paclitaxel: CT, clinical trial  
 paclitaxel: CM, drug comparison  
 paclitaxel: DT, drug therapy  
 paclitaxel: PD, pharmacology  
 paclitaxel poliglumex: CT, clinical trial  
 paclitaxel poliglumex: DT, drug therapy  
 paclitaxel poliglumex: PD, pharmacology  
 pemetrexed  
 pk 166  
 platinum derivative: AE, adverse drug reaction  
 platinum derivative: CM, drug comparison  
 platinum derivative: DT, drug therapy  
 platinum derivative: PD, pharmacology  
 proteasome inhibitor: CT, clinical trial  
 proteasome inhibitor: DT, drug therapy  
 proteasome inhibitor: PD, pharmacology  
 raloxifene: DT, drug therapy  
 raloxifene: PD, pharmacology  
 retinoid derivative: DT, drug therapy  
 retinoid derivative: PD, pharmacology  
 rpr 109881a  
 rpr 116258a  
 sorafenib  
 tamoxifen: CT, clinical trial  
 tamoxifen: CM, drug comparison  
 tamoxifen: DT, drug therapy  
 tamoxifen: PD, pharmacology  
 taxane derivative: CT, clinical trial  
 taxane derivative: CB, drug combination  
 taxane derivative: DT, drug therapy  
 taxane derivative: PD, pharmacology  
 temsirolimus  
 tipifarnib  
 toremifene: DT, drug therapy  
 toremifene: PD, pharmacology  
 trabectedin: AE, adverse drug reaction

trabectedin: CT, clinical trial  
 trabectedin: DT, drug therapy  
 trabectedin: PD, pharmacology  
 trastuzumab: CT, clinical trial  
 trastuzumab: DT, drug therapy  
 trastuzumab: PD, pharmacology  
 unclassified drug  
 unindexed drug  
 vinflunine: AE, adverse drug reaction  
 vinflunine: CT, clinical trial  
 vinflunine: DT, drug therapy  
 vinflunine: PD, pharmacology

RN (3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide)  
 443912-23-0; (arzoixifene) 182133-25-1, 182133-27-3; (bortezomib)  
 179324-69-7, 197730-97-5; (canertinib) 267243-28-7, 289499-45-2,  
 338796-35-3; (cgp 69846a) 177075-18-2; (cm 101) 188417-67-6; (docetaxel)  
 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib)  
 183319-69-9, 183321-74-6; (fulvestrant) 129453-61-8; (gefitinib)  
 184475-35-2, 184475-55-6, 184475-56-7; (ixabepilone) 219989-84-1;  
 (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lenalidomide)  
 191732-72-6; (letrozole) 112809-51-5; (lonafarnib) 193275-84-2;  
 (marimastat) 154039-60-8; (navelbine) 71486-22-1; (paclitaxel poliglumex)  
 263351-82-2; (paclitaxel) 33069-62-4; (pemetrexed) 137281-23-3,  
 150399-23-8; (raloxifene) 82640-04-8, 84449-90-1; (sorafenib)  
 284461-73-0; (tamoxifen) 10540-29-1; (temsirolimus) 162635-04-3,  
 343261-52-9; (tipifarnib) 192185-72-1; (toremifene) 89778-26-7;  
 (trabectedin) 114899-77-3; (trastuzumab) 180288-69-1; (vinflunine)  
 162652-95-1

CN abi 007; alimta; bay 439006; bb 2516; bms 184476; bms 247550; caelyx; cc  
 4047; cc 5013; cc 7085; cci 779; cdc 801; ci 1033; cm 101; ct 2103; et  
 743; faslodex; gw 2016; herceptin; isis 5132; myocet; osi 774; pk 166; ps  
 341; r 115777; rpr 109881a; rpr 116258a; sch 66336; taxotere; zd 1839

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ACCESSION NUMBER: 2003091304 EMBASE Full-text  
 TITLE: Protein kinase inhibitors from the urea class.  
 AUTHOR: Dumas, Jacques (correspondence)  
 CORPORATE SOURCE: Bayer Research Center, Bayer Corporation, Pharmaceutical Division, 400 Morgan Lane, West Haven, CT 06516, United States. jacques.dumas.b@bayer.com  
 SOURCE: Current Opinion in Drug Discovery and Development, (Sep 2002) Vol. 5, No. 5, pp. 718-727.  
 Refs: 74  
 ISSN: 1367-6733 CODEN: CODDFP  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 016 Cancer  
 029 Clinical and Experimental Biochemistry  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 25 Mar 2003  
 Last Updated on STN: 25 Mar 2003

AB Protein kinase inhibitors hold great potential as novel therapies for cancer and inflammatory disorders. While bis-aryl ureas have been reported as kinase inhibitors as early as 1996, a number of publications and patent applications appeared in the literature during the past two years. Three urea-based kinase

inhibitors are currently undergoing clinical trials. The present review summarizes available data, and provides an overview of the structure-activity relationships against a variety of kinase targets, including p38, Raf-1 and cyclin-dependent kinases.

CT Medical Descriptors:

\*angiogenesis  
animal model  
antiinflammatory activity  
antineoplastic activity  
arthritis: DT, drug therapy  
cancer chemotherapy  
\*cell cycle  
clinical trial  
diarrhea: SI, side effect  
drug efficacy  
drug protein binding  
drug research  
drug safety  
drug structure  
drug targeting  
\*enzyme inhibition  
fatigue: SI, side effect  
human  
human cell  
inflammation  
kidney carcinoma: DT, drug therapy  
liver cell carcinoma: DT, drug therapy  
mouse  
nonhuman  
phase 1 clinical trial  
phase 2 clinical trial  
rash: SI, side effect  
review  
structure activity relation

CT Drug Descriptors:

\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: CT, clinical trial  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: AD, drug administration  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: AN, drug analysis  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: CR, drug concentration  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: DV, drug development  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: DO, drug dose  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: DT, drug therapy  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: PO, oral drug administration  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: PK, pharmacokinetics  
\*3 (4 bromo 2,6 difluorobenzoyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4  
isothiazolecarboxamide: PD, pharmacology  
4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl]  
3 butyn 1 ol  
5 (2,6 dichlorophenyl) 2 (2,4 difluorophenylthio)pyrimido[1,6 b]pyridazin  
6 one: DV, drug development  
antiinflammatory agent: CT, clinical trial

antiinflammatory agent: AD, drug administration  
 antiinflammatory agent: AN, drug analysis  
 antiinflammatory agent: DV, drug development  
 antiinflammatory agent: DO, drug dose  
 antiinflammatory agent: DT, drug therapy  
 antiinflammatory agent: IV, intravenous drug administration  
 antiinflammatory agent: PD, pharmacology  
 \*cyclin dependent kinase inhibitor: CT, clinical trial  
 \*cyclin dependent kinase inhibitor: AN, drug analysis  
 \*cyclin dependent kinase inhibitor: DV, drug development  
 \*cyclin dependent kinase inhibitor: PD, pharmacology  
 \*dorapimod: CT, clinical trial  
 \*dorapimod: AN, drug analysis  
 \*dorapimod: DV, drug development  
 \*dorapimod: DO, drug dose  
 \*dorapimod: DT, drug therapy  
 \*dorapimod: IV, intravenous drug administration  
 \*dorapimod: PD, pharmacology  
 enzyme inhibitor: AE, adverse drug reaction  
 enzyme inhibitor: CT, clinical trial  
 enzyme inhibitor: AN, drug analysis  
 enzyme inhibitor: CR, drug concentration  
 enzyme inhibitor: DV, drug development  
 enzyme inhibitor: DO, drug dose  
 enzyme inhibitor: DT, drug therapy  
 enzyme inhibitor: PK, pharmacokinetics  
 enzyme inhibitor: PD, pharmacology  
 epidermal growth factor receptor kinase  
 erlotinib: CT, clinical trial  
 flavopiridol: CT, clinical trial  
 gefitinib: CT, clinical trial  
 imatinib: CT, clinical trial  
 mitogen activated protein kinase inhibitor: CT, clinical trial  
 mitogen activated protein kinase inhibitor: AN, drug analysis  
 mitogen activated protein kinase inhibitor: DV, drug development  
 mitogen activated protein kinase inhibitor: PD, pharmacology  
 \*protein kinase inhibitor: AE, adverse drug reaction  
 \*protein kinase inhibitor: CT, clinical trial  
 \*protein kinase inhibitor: AD, drug administration  
 \*protein kinase inhibitor: AN, drug analysis  
 \*protein kinase inhibitor: CR, drug concentration  
 \*protein kinase inhibitor: DV, drug development  
 \*protein kinase inhibitor: DO, drug dose  
 \*protein kinase inhibitor: DT, drug therapy  
 \*protein kinase inhibitor: IV, intravenous drug administration  
 \*protein kinase inhibitor: PO, oral drug administration  
 \*protein kinase inhibitor: PK, pharmacokinetics  
 \*protein kinase inhibitor: PD, pharmacology  
   protein tyrosine kinase inhibitor: CT, clinical trial  
   protein tyrosine kinase inhibitor: AN, drug analysis  
   protein tyrosine kinase inhibitor: DV, drug development  
   protein tyrosine kinase inhibitor: PD, pharmacology  
 quinazoline derivative: DV, drug development  
 ruboxistaurin: DV, drug development  
 rw 67657: DV, drug development  
 \*sorafenib: AE, adverse drug reaction  
 \*sorafenib: CT, clinical trial  
 \*sorafenib: AD, drug administration  
 \*sorafenib: AN, drug analysis  
 \*sorafenib: DV, drug development

\*sorafenib: DO, drug dose  
 \*sorafenib: DT, drug therapy  
 \*sorafenib: PO, oral drug administration  
 \*sorafenib: PD, pharmacology  
 unclassified drug  
 \*urea derivative: AE, adverse drug reaction  
 \*urea derivative: CT, clinical trial  
 \*urea derivative: AD, drug administration  
 \*urea derivative: AN, drug analysis  
 \*urea derivative: CR, drug concentration  
 \*urea derivative: DV, drug development  
 \*urea derivative: DO, drug dose  
 \*urea derivative: DT, drug therapy  
 \*urea derivative: IV, intravenous drug administration  
 \*urea derivative: PO, oral drug administration  
 \*urea derivative: PK, pharmacokinetics  
 \*urea derivative: PD, pharmacology

RN (3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide) 252003-65-9; (4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl] 3 butyn 1 ol) 215303-72-3; (doramapimod) 285983-48-4; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5, 146426-40-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (ruboxistaurin) 169939-93-9, 169939-94-0; (sorafenib) 284461-73-0

CN (1) bay 43 9006; (2) birb 796; (3) cp 547632; (4) ly 333531; (5) osi 774; (6) rwj 67657; (7) vx 745; (8) zd 1839; glivec

CO (1) Bayer; (2) Boehringer Ingelheim; (3) Pfizer; (4) Lilly; (5) Osi; (6) RW Johnson; (7) Vertex; (8) Astra Zeneca; Amgen; Aventis; Banyu; BASF; Glaxo SmithKline; Pharmacia Upjohn; Sugen

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ACCESSION NUMBER: 2002326813 EMBASE Full-text  
 TITLE: The chemistry of biological processes: Editorial overview.  
 AUTHOR: McAlpine, James (correspondence); Culver, Kenneth; Ecker, David  
 CORPORATE SOURCE: Phytera Inc., 377 Plantation Street, Worcester, MA 01605, United States. aandjmc@alpine@yahoo.com  
 SOURCE: Current Opinion in Drug Discovery and Development, (Mar 2002) Vol. 5, No. 2, pp. 191-193.  
 ISSN: 1367-6733 CODEN: CODDFE  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Editorial  
 FILE SEGMENT: 037 Drug Literature Index  
 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 3 Oct 2002  
 Last Updated on STN: 3 Oct 2002

CT Medical Descriptors:  
 Bifidobacterium  
 Clostridium  
 DNA vector  
 drug activity  
 \*drug development  
 drug screening  
 editorial  
 Salmonella

CT Drug Descriptors:

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid  
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2  
 thienylsulfonyl) 1h 1,4 benzodiazepine  
 6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3  
 d]pyrimidine

adl 681  
 angiogenesis inhibitor  
 antibiotic agent  
 antineoplastic agent  
 bim 46228  
 canertinib  
 cyclin dependent kinase inhibitor  
 epidermal growth factor receptor  
 erlotinib  
 fluorouracil  
 gefitinib  
 imatinib  
 lb 42908  
 lonafarnib  
 nl 2001  
 paclitaxel  
 pelitinib  
 phosphotransferase inhibitor  
 protein kinase C inhibitor  
 protein tyrosine kinase inhibitor  
 recombinant antibody  
 semaxanib  
 sorafenib  
 tipifarnib  
 unclassified drug  
 unindexed drug  
 vancomycin  
 vandetanib  
 vatalanib

- RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid)  
 252916-29-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4  
 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9,  
 195987-41-8; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3;  
 (erlotinib) 183319-69-9, 183321-74-6; (fluorouracil) 51-21-8; (gefitinib)  
 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5,  
 220127-57-1; (lonafarnib) 193275-84-2; (paclitaxel) 33069-62-4;  
 (pelitinib) 257933-82-7; (semaxanib) 186610-95-7; (sorafenib)  
 284461-73-0; (tipifarnib) 192185-72-1; (vancomycin) 1404-90-6,  
 1404-93-9; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib)  
 212141-54-3, 212142-18-2
- CN (1) adl 681; (2) bay 439006; (3) bim 46228; (4) bms 214662; (5) ci 1033;  
 (6) ekb 569; (7) lb 42908; (8) nl 2001; (9) osi 774; (10) pki 166; (11)  
 ptk 787; (12) r 115777; (13) sch 66336; (14) sti 571; (15) su 5416; (16)  
 su 6668; (17) zd 1839; (18) zd 6474; taxol
- CO (1) Novartis; (2) Bayer; (3) Biomeasure; (4) Bristol Myers Squibb; (5)  
 Pfizer; (6) Wyeth Ayerst; (7) LG Chemical; (8) Nuoncology; (9) Osi; (10)  
 Novartis; (11) Novartis; (12) Janssen; (13) Schering Plough; (14) Gleevec;  
 (15) Sugen; (16) Sugen; (17) Astra Zeneca; (18) Astra Zeneca

L110 ANSWER 84 OF 84 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights  
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ACCESSION NUMBER: 2002194397 EMBASE [Full-text](#)

TITLE: IDdb News focus.

SOURCE: Current Drug Discovery, (2002) No. MAY, pp. 13-16.  
 ISSN: 1472-7463 CODEN: CDDUAI

COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Note  
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 016 Cancer  
 031 Arthritis and Rheumatism  
 037 Drug Literature Index  
 004 Microbiology: Bacteriology, Mycology, Parasitology  
 and Virology  
 008 Neurology and Neurosurgery  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 13 Jun 2002  
 Last Updated on STN: 13 Jun 2002

CT Medical Descriptors:  
 alcoholism: DT, drug therapy  
 allergic rhinitis: DT, drug therapy  
 anemia: DT, drug therapy  
 anxiety neurosis: DT, drug therapy  
 asthma: DT, drug therapy  
 bladder disease: DT, drug therapy  
 \*cancer: DT, drug therapy  
 cataplexy: DT, drug therapy  
 clinical trial  
 condyloma: DT, drug therapy  
 controlled study  
 drug approval  
 drug design  
 drug indication  
 drug manufacture  
 drug marketing  
 drug structure  
 heart failure: DT, drug therapy  
 human  
 influenza: DT, drug therapy  
 influenza: PC, prevention  
 kidney cancer: DT, drug therapy  
 narcolepsy: DT, drug therapy  
 non insulin dependent diabetes mellitus: DT, drug therapy  
 nonhodgkin lymphoma: DT, drug therapy  
 nose congestion: DT, drug therapy  
 note  
 osteoarthritis: DT, drug therapy  
 papilloma: DT, drug therapy  
 patent  
 rheumatoid arthritis: DT, drug therapy  
 \*stroke: DT, drug therapy  
 thromboembolism: DT, drug therapy  
 thromboembolism: PC, prevention  
 \*virus infection: DT, drug therapy  
 Wart virus  
 CT Drug Descriptors:  
 alpha adrenergic receptor stimulating agent: CB, drug combination  
 alpha adrenergic receptor stimulating agent: DT, drug therapy  
 antisense oligonucleotide: CT, clinical trial  
 antisense oligonucleotide: DT, drug therapy  
 apoptosis inhibitor: DT, drug therapy  
 arixta  
 beta 3 adrenergic receptor stimulating agent: CT, clinical trial  
 beta 3 adrenergic receptor stimulating agent: DT, drug therapy  
 bucindolol  
 camptothecin derivative: CT, clinical trial



camptothecin derivative: DT, drug therapy  
 carboxylic acid derivative: DT, drug therapy  
 celecoxib: DT, drug therapy  
 chir 200131  
 desloratadine: DT, drug therapy  
 DNA: CT, clinical trial  
 DNA: CB, drug combination  
 DNA: DT, drug therapy  
 epi 2010  
 fondaparinux: DT, drug therapy  
 histamine H1 receptor antagonist: CB, drug combination  
 histamine H1 receptor antagonist: DT, drug therapy  
 histamine H3 receptor agonist: DT, drug therapy  
 influenza vaccine: CT, clinical trial  
 influenza vaccine: DT, drug therapy  
 interleukin 2 receptor antibody: CT, clinical trial  
 interleukin 2 receptor antibody: DT, drug therapy  
 krp 199  
 loratadine: DT, drug therapy  
 naltrexone derivative: CT, clinical trial  
 naltrexone derivative: DT, drug therapy  
 ori 1001  
 ortataxel  
 oxybate sodium: DT, drug therapy  
 oxybutynin: CT, clinical trial  
 oxybutynin: DT, drug therapy  
 oxybutynin: TD, transdermal drug administration  
 phosphotransferase inhibitor: CT, clinical trial  
 phosphotransferase inhibitor: DT, drug therapy  
 phosphotransferase inhibitor: PO, oral drug administration  
 protein tyrosine kinase inhibitor: DV, drug development  
 protein tyrosine kinase inhibitor: DT, drug therapy  
 recombinant erythropoietin: DV, drug development  
 recombinant erythropoietin: DT, drug therapy  
 rituximab: CT, clinical trial  
 rituximab: CB, drug combination  
 rituximab: DT, drug therapy  
 rosiglitazone: DT, drug therapy  
 sb 418790  
 serine proteinase inhibitor: DV, drug development  
 serine proteinase inhibitor: DT, drug therapy  
 solabegron  
 sorafenib  
 ta hpv  
 taxane derivative: CT, clinical trial  
 taxane derivative: DT, drug therapy  
 unclassified drug  
 unindexed drug  
 uridine derivative: CT, clinical trial  
 uridine derivative: DT, drug therapy  
 valdecoxib: DT, drug therapy  
 vasopressin receptor antagonist: CT, clinical trial  
 vasopressin receptor antagonist: DT, drug therapy  
 virus vaccine: CT, clinical trial  
 virus vaccine: DV, drug development  
 virus vaccine: DT, drug therapy  
 wk 175  
 wx uk 1

RN (bucindolol) 71119-11-4; (celecoxib) 169590-42-5; (desloratadine)  
 100643-71-8; (DNA) 9007-49-2; (fondaparinux) 104993-28-4, 114870-03-0;

(interleukin 2 receptor antibody) 179045-86-4; (loratadine) 79794-75-5; (ortataxel) 186348-05-0, 186348-23-2; (oxybate sodium) 502-85-2; (oxybutynin) 1508-65-2, 5633-20-5; (recombinant erythropoietin) 113427-24-0, 122312-54-3, 130455-76-4; (rituximab) 174722-31-7; (rosiglitazone) 122320-73-4, 155141-29-0; (solabegron) 252920-94-8, 451470-34-1; (sorafenib) 234461-73-0; (valdecixib) 181695-72-7

- CN (1) arixta; (2) arixta; (3) avandia; (4) bay 439006; (5) bextra; (6) bextra; (7) celebrex; (8) celebrex; (9) chir 200131; (10) clarinex; (11) claritin; (12) epi 2010; (13) gw 427353; (14) idn 5109; (15) krp 199; (16) ori 1001; (17) oxytrol; (18) rituxan; (19) sb 418790; (20) ta hpv; (21) wk 175; (22) wx uk 1; (23) xyrem
- CO (1) Organon; (2) Sanofi Synthelabo; (3) Glaxo SmithKline; (4) Bayer; (5) Pfizer; (6) Pharmacia; (7) Pfizer; (8) Pharmacia; (9) Chiron; (10) Schering Plough; (11) Schering Plough; (12) epigenesis; (13) Glaxo SmithKline; (14) Bayer; (15) Kyorin; (16) OriGenix Technologies; (17) Watson; (18) Dynavax; (19) Glaxo SmithKline; (20) Xenova; (21) Wilex Biotechnology; (22) Wilex Biotechnology; (23) Orphan

=> d his nofile

(FILE 'HOME' ENTERED AT 10:58:16 ON 16 JUL 2008)

FILE 'HCAPLUS' ENTERED AT 10:58:27 ON 16 JUL 2008

L1 1 SEA ABB=ON PLU=ON US20070142440/PN  
D IBIB AB IT SC  
SEL RN

FILE 'REGISTRY' ENTERED AT 10:59:13 ON 16 JUL 2008

L2 47 SEA ABB=ON PLU=ON (102-56-7/BI OR 1199-46-8/BI OR 139691-76-2  
/BI OR 144697-16-5/BI OR 150027-19-3/BI OR 176977-85-8/BI OR  
19438-10-9/BI OR 220000-87-3/BI OR 2835-98-5/BI OR 28443-50-7/B  
I OR 349-65-5/BI OR 372092-80-3/BI OR 400-99-7/BI OR 43115-40-8  
/BI OR 446-36-6/BI OR 454-81-9/BI OR 53981-24-1/BI OR 67-56-1/B  
I OR 74-89-5/BI OR 771-61-9/BI OR 7719-09-7/BI OR 80449-02-1/BI  
OR 827025-41-2/BI OR 827025-43-4/BI OR 856424-02-7/BI OR  
864291-02-1/BI OR 864291-04-3/BI OR 864291-06-5/BI OR 864291-08  
-7/BI OR 864291-10-1/BI OR 864291-12-3/BI OR 864291-14-5/BI OR  
864291-16-7/BI OR 864291-18-9/BI OR 864291-20-3/BI OR 864291-22  
-5/BI OR 864291-24-7/BI OR 864291-26-9/BI OR 864291-28-1/BI OR  
864291-32-7/BI OR 864291-34-9/BI OR 864291-39-4/BI OR 95-03-4/B  
I OR 95-55-6/BI OR 95-84-1/BI OR 98-98-6/BI OR 99-76-3/BI)  
L3 STRUCTURE UPLOADED  
D  
L4 1 SEA SSS SAM L3  
D SCAN  
L5 14 SEA ABB=ON PLU=ON L2 AND 3/N  
L6 0 SEA ABB=ON PLU=ON L2 AND 4/N

FILE 'STNGUIDE' ENTERED AT 11:03:11 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 11:04:56 ON 16 JUL 2008

L7 STRUCTURE UPLOADED  
L8 SCR 2043 AND 1918  
L9 3 SEA SSS SAM L7 NOT L8  
L10 16 SEA ABB=ON PLU=ON L2 AND 3-9/NR  
D SCAN

FILE 'STNGUIDE' ENTERED AT 11:39:41 ON 16 JUL 2008  
D COST

FILE 'REGISTRY' ENTERED AT 11:50:36 ON 16 JUL 2008

L11 STRUCTURE UPLOADED  
D  
L12 25 SEA SSS SAM L11 NOT L8  
L13 SCR 2021  
L14 33 SEA SSS SAM L11 AND L13 NOT L8  
L15 SCR 1995 OR 2021  
L16 30 SEA SSS SAM L11 AND L15 NOT L8  
L17 SCR 1841  
L18 50 SEA SSS SAM L11 AND L17 NOT L8

FILE 'STNGUIDE' ENTERED AT 11:55:43 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 11:56:29 ON 16 JUL 2008

L19 STRUCTURE UPLOADED  
D

L20 50 SEA SSS SAM L19 NOT L8  
 L21 50 SEA SSS SAM L19 AND L17 NOT L8  
 L22 SCR 2043 AND 1918 AND 1842  
 L23 48 SEA SSS SAM L19 NOT L22  
 L24 47 SEA ABB=ON PLU=ON L2 NOT 30-99/C  
 L25 47 SEA ABB=ON PLU=ON L2 NOT 35-99/C

FILE 'STNGUIDE' ENTERED AT 12:06:12 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:08:16 ON 16 JUL 2008  
 L26 STRUCTURE UPLOADED  
 D  
 L27 50 SEA SSS SAM L26 NOT L22  
 L28 50 SEA SSS SAM L26 AND L15 NOT L22  
 L29 SCR 2043 AND 1918 AND 1842 AND 2016  
 L30 50 SEA SSS SAM L26 AND L15 NOT L29  
 L31 STRUCTURE UPLOADED  
 D  
 L32 35 SEA SSS SAM L31 NOT L22  
 L33 35 SEA SSS SAM L31 AND L15 NOT L22  
 L34 36 SEA SSS SAM L31 AND L15 NOT L29

FILE 'STNGUIDE' ENTERED AT 12:30:14 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:38:18 ON 16 JUL 2008  
 L35 STRUCTURE UPLOADED  
 L36 50 SEA SSS SAM L35 AND L15 NOT L29

FILE 'STNGUIDE' ENTERED AT 12:39:05 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:40:08 ON 16 JUL 2008  
 L37 STRUCTURE UPLOADED  
 D  
 L38 50 SEA SSS SAM L37 AND L15 NOT L29  
 L39 SCR 2043 AND 1918 AND 2050 AND 1842 AND 2016  
 L40 50 SEA SSS SAM L37 AND L15 NOT L39  
 L41 SCR 1995 OR 2021 OR 1841  
 L42 50 SEA SSS SAM L37 AND L41 NOT L39

FILE 'STNGUIDE' ENTERED AT 12:49:58 ON 16 JUL 2008

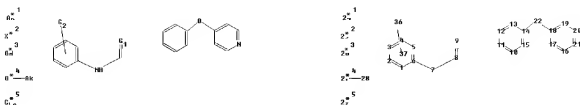
FILE 'STNGUIDE' ENTERED AT 12:54:24 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 12:54:29 ON 16 JUL 2008  
 L43 STRUCTURE UPLOADED  
 D  
 L44 50 SEA SSS SAM L43 AND L41 NOT L39  
 L45 STRUCTURE UPLOADED  
 D  
 L46 50 SEA SSS SAM L45 AND L41 NOT L39

FILE 'STNGUIDE' ENTERED AT 13:03:34 ON 16 JUL 2008

FILE 'REGISTRY' ENTERED AT 13:17:03 ON 16 JUL 2008  
 L47 STRUCTURE UPLOADED  
 D

Uploading L11.str



```

chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-
21
17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 7-8 8-9 14-22 18-22 27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-
21
17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 : 10 : 16 :

```

G1:O,S

G2:[\*1],[\*2],[\*3],[\*4],[\*5]

Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

```

```

L48          SCR 2043 AND 1918 AND 2050
L49          50 SEA SSS SAM L47 NOT L48
L50          1662 SEA SSS FUL L47 NOT L48
L51          14 SEA ABB=ON PLU=ON L50 AND L2
              SAVE TEMP L50 NAT724REGL1/A

```

FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008

```

L52          607 SEA ABB=ON PLU=ON L50
L53          584 SEA ABB=ON PLU=ON L52 AND PHARMAC7/SC,SX
L54          64 SEA ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004 OR PRY<2004)
L55          0 SEA ABB=ON PLU=ON L54 AND L1

```

```

E TYROSINE KINASE RECEPTORS/CT
E E3+ALL
L56      2011 SEA ABB=ON PLU=ON "TYROSINE KINASE RECEPTORS"+UF/CT
L57      20 SEA ABB=ON PLU=ON L56 AND L52
L58      63 SEA ABB=ON PLU=ON L54 NOT L57
L59      334654 SEA ABB=ON PLU=ON TYROSINE KINASE? OR KINASE? OR KINASE
        INHIB?
L60      3212 SEA ABB=ON PLU=ON TIE(W)2 OR TIE2 OR VEGRF OR RAF KINASE?
L61      335008 SEA ABB=ON PLU=ON L59 OR L60
L62      382 SEA ABB=ON PLU=ON L52 AND L61
L63      382 SEA ABB=ON PLU=ON L52 AND L61
L64      1797 SEA ABB=ON PLU=ON (TIE2 OR TIE(W)2 OR VEGFR OR RAF) (W)
        (KINASE? OR KINASE INHIB?)
L65      114 SEA ABB=ON PLU=ON L52 AND L64
L66      52 SEA ABB=ON PLU=ON L63 AND (AY<2004 OR PY<2004 OR PRY<2004)
L67      35 SEA ABB=ON PLU=ON L65 AND (AY<2004 OR PY<2004 OR PRY<2004)
L68      31 SEA ABB=ON PLU=ON L54 NOT L67
        SAVE TEMP L54 NAT724HCAP/A
L69      22 SEA ABB=ON PLU=ON BURGDORF L7/AU
L70      45 SEA ABB=ON PLU=ON BUCHSTALLER H7/AU
L71      36 SEA ABB=ON PLU=ON STIEBER F7/AU
L72      28 SEA ABB=ON PLU=ON AMENDT C7/AU
L73      202 SEA ABB=ON PLU=ON GREINER H7/AU
L74      150 SEA ABB=ON PLU=ON GRELL M7/AU
L75      38 SEA ABB=ON PLU=ON SIRRENBERG C7/AU
L76      3 SEA ABB=ON PLU=ON ZENKE K7/AU
L77      10 SEA ABB=ON PLU=ON ((L69 OR L70 OR L71 OR L72 OR L73 OR L74
        OR L75 OR L76)) AND L52) OR (L1 AND L52)
L78      5 SEA ABB=ON PLU=ON L77 NOT L54
        SAVE TEMP L78 NAT724HCAIN/A

FILE 'REGISTRY' ENTERED AT 13:38:42 ON 16 JUL 2008
L79      1 SEA ABB=ON PLU=ON L50 AND (MEDLINE/LC OR BIOSIS/LC OR
        DRUGU/LC OR EMBASE/LC)

FILE 'MEDLINE' ENTERED AT 13:39:09 ON 16 JUL 2008
L80      0 SEA ABB=ON PLU=ON L79

FILE 'BIOSIS' ENTERED AT 13:39:15 ON 16 JUL 2008
L81      89 SEA ABB=ON PLU=ON L79
L82      34 SEA ABB=ON PLU=ON L81 AND L64
L83      3 SEA ABB=ON PLU=ON L82 AND (PREP? OR SYNTHES?)
        D TI 1-3
L84      0 SEA ABB=ON PLU=ON L82 AND ANGIOGENESIS INHIB?
L85      6 SEA ABB=ON PLU=ON L82 AND TYROSINE KINASE?
L86      8 SEA ABB=ON PLU=ON L83 OR L85

FILE 'DRUGU' ENTERED AT 13:42:12 ON 16 JUL 2008
L87      0 SEA ABB=ON PLU=ON L79

FILE 'EMBASE' ENTERED AT 13:42:27 ON 16 JUL 2008
L88      2050 SEA ABB=ON PLU=ON L79
L89      605 SEA ABB=ON PLU=ON L88 AND TYROSINE KINASE?
L90      1 SEA ABB=ON PLU=ON L88 AND TYROSIN KINASE INHIB?
L91      165 SEA ABB=ON PLU=ON L88 AND L64
L92      1332 SEA ABB=ON PLU=ON RAF KINASE?
L93      164 SEA ABB=ON PLU=ON L92 AND L88
        D TI L90
L94      26 SEA ABB=ON PLU=ON L89 AND (PREPARAT? OR SYNTHES?)
        D TI KWIC 1-4

```

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L95      26 SEA ABB=ON   PLU=ON   L94 AND (PHARMAC? OR THERAP?)
L96      27 SEA ABB=ON   PLU=ON   L90 OR L94
L97      0 SEA ABB=ON   PLU=ON   L96 AND (AY<2004 OR PY<2004 OR PRY<2004)
L98      12 SEA ABB=ON   PLU=ON   L89 AND (AY<2004 OR PY<2004 OR PRY<2004)

      FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:48:43 ON 16 JUL 2008
L99      0 SEA ABB=ON   PLU=ON   BURGDORF LARS/AU
L100     9 SEA ABB=ON   PLU=ON   BUCHSTALLER HANS PETER/AU
L101     8 SEA ABB=ON   PLU=ON   STIEBER FRANK/AU
L102     7 SEA ABB=ON   PLU=ON   AMENDT CHRISTIANE/AU
L103    14 SEA ABB=ON   PLU=ON   GREINER HARTMUT/AU
L104    70 SEA ABB=ON   PLU=ON   GRELL MATTHIAS/AU
L105    19 SEA ABB=ON   PLU=ON   SIRRENBERG CHRISTIAN/AU
L106     2 SEA ABB=ON   PLU=ON   ZENKE FRANK/AU
L107     3 SEA ABB=ON   PLU=ON   ((L100 OR L101 OR L102 OR L103 OR L104 OR
      L105 OR L106)) AND TYROSINE KINASE?
L108     0 SEA ABB=ON   PLU=ON   ((L100 OR L101 OR L102 OR L103 OR L104 OR
      L105 OR L106)) AND L64

      FILE 'STNGUIDE' ENTERED AT 13:52:17 ON 16 JUL 2008
      D COST
      D QUE L78
      D QUE L107

      FILE 'HCAPLUS, MEDLINE, EMBASE' ENTERED AT 13:53:35 ON 16 JUL 2008
L109     8 DUP REM L78 L107 (0 DUPLICATES REMOVED)
      ANSWERS '1-5' FROM FILE HCAPLUS
      ANSWERS '6-7' FROM FILE MEDLINE
      ANSWER '8' FROM FILE EMBASE
      D L109 1-5 IBIB ABS
      D L109 6-8 IBIB AB
      D QUE L54
      D QUE L86
      D QUE L98

      FILE 'HCAPLUS, BIOSIS, EMBASE' ENTERED AT 13:54:57 ON 16 JUL 2008
L110    84 DUP REM L54 L86 L98 (0 DUPLICATES REMOVED)
      ANSWERS '1-64' FROM FILE HCAPLUS
      ANSWERS '65-72' FROM FILE BIOSIS
      ANSWERS '73-84' FROM FILE EMBASE
      D L110 1-64 IBIB ABS FHITSTR HITIND
      D L110 65-84 IBIB AB HITIND

```